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THE HUMAN CORPUS LUTEUM OF PREGNANCY

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A CORPUS luteum is found only in the ovary of mammals. Subsequent to the classical experiments of Fraenkel (1903), who demonstrated that the corpus luteum plays an important part in maintaining gestation in the rabbit, attention was rapidly diverted from the anatomy to the dynamic and perhaps more spectacular physiology of this body. This diversion has culminated in the isolation of progesterone and the techniques for assaying this hormone.

The structure of the human corpus luteum of pregnancy was being investigated in the first two decades of the present century by Rabl (1899), Seitz (1906), Meyer (1911), Miller (1914), and Marcotty (1914), but there has been no anatomical report since the comprehensive study of Moulonguet-Doleris (1925).

Investigations into the ovarian hormones have been in progress in this department of anatomy since 1932. When it was discovered that the human corpus luteum of early pregnancy was a cystic structure and that the cystic cavity contained a potent hormonal fluid (Gillman and Smyth, 1939) it was obvious that re-examination of the histology of the gravid human corpus luteum was also overdue. The anatomical approach, while laborious, was imperative if we were to correlate changes in structure with those of function in the human corpus luteum. This study was facilitated by accumulating a comprehensive series of fresh human corpora lutea, removed at operation from cases of proved intra-uterine pregnancy at different stages of gestation.

In this paper we hope to demonstrate that there is a "critical period" of sudden growth in the volume of the corpus luteum between the fiftieth and sixtieth days of pregnancy due to an excess production of hormonal fluid in the fibrous-tissue-lined cavity, which is subsequently obliterated; that the theca-lutein cells attain their maximum development synchronously with the development of this curious cavity and that subsequent upon its collapse they too disappear; that the granulosa-lutein cells on the other hand persist throughout pregnancy and that their vacuolar secretion may degenerate into colloid and even solid calcium containing deposit. Curves will be presented displaying the relative incidence of cells containing lipoid, secretory granules, and colloid at the various stages of pregnancy typified by our specimens. Finally we have correlated the experimental, physiological, and cytological evidence bearing on the function of the corpus luteum of pregnancy.

MATERIAL AND METHODS

The corpora lutea from normal cases of intra-uterine pregnancy used in this study

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TABLE I.—NUMBER AND DISTRIBUTION OF CASES OF GRAVID CORPORA LUTEA EXAMINED BY VARIOUS INVESTIGATORS

Author	Year	Operation specimens		Autopsy specimens	Total examined
		Intra-uterine	Extra-uterine		
Meyer	1911				12**
Miller	1914				28‡‡
Marcotty	1914	15	4	7	28*
Moulonguet-Doleris	1925	6‡	9		15
Portes, Aschheim and Robey	1938				?§
Present authors		13	2	4	19

*Marcotty. In two cases no data as to the origin of the specimen are available.
**2 to 5 months.
‡Moulonguet-Doleris. It is not indicated whether these are all operation cases.
‡‡Operative.
§Portes, Aschheim and Robey. No exact figures are given.

represent one of the largest series hitherto examined (Table I). With the exception of Marcotty, investigators have not always divulged the source of their material and thus we are ignorant as to whether the corpora were removed at operation from individuals who had a normal intra-uterine pregnancy or ectopic pregnancy, or whether the ovaries may not have been removed at autopsy.

We have found that corpora lutea removed from cases of intra-uterine and of ectopic pregnancy are not identical in structure since the corpus luteum undergoes involution when the embryo dies and it is unusual to find a living embryo in an ectopic pregnancy.

Again, in autopsy cases, as hereinafter indicated, the lipoid and colloid disappear from the corpus luteum. Specimens examined 24 hours after death present scarcely any colloid.

We described here, therefore, only such corpora lutea as were removed at operation in cases of a proved intra-uterine pregnancy. The few autopsy and extra-uterine specimens are included in Table I only for comparison.

Of our 19 specimens no less than 13 were removed at operation from normal individuals in different stages of intra-uterine pregnancy, 2 were from operations for ectopic gestation, and 4 were from autopsies. Three of the autopsy specimens were from cases of accidental death and the fourth from a case dying of puerperal sepsis. Table II shows the distribution of our cases under three classes, namely: (a) normal intra-uterine cases in which specimens were removed at operation, (b) ectopic cases in which specimens were obtained at operation, and (c) autopsy cases.

The age of the corpus luteum in operative cases has been estimated from the date of the last menstrual period, and in the autopsy cases from the size of the fetus according to the data collated by Arey (1930).

The specimens were fixed in 20 per cent neutral formol and in addition small pieces were removed for cytological investigation, the description of which will be published elsewhere. Fragments of the formol-fixed portions were subjected to the freezing microtome and sections cut for the investigation of lipoid, while the remainder of the specimen was dehydrated in alcohol and embedded in paraffin.

The frozen sections of each specimen were stained in routine fashion by the scharlach R, Nile blue sulphate, and osmium tetroxide methods for the detection of lipoid and fatty acids. A fourth section was stained with scharlach R and counterstained by hematoxylin, while a fifth section was mounted in glycerine without staining and examined by means of polarized light for the detection of anisotropic lipoid. Other sections were subjected to the Schultz microchemical technique for cholesterol. A concise description of these lipoid methods is given by Carleton (1938) and was critically discussed for the gall bladder by Stein (1938).

The paraffin sections were stained as a routine with hematoxylin and eosin, with Mallory's triple connective tissue stain, by the Bielschowsky-Foot method for reticulum, and with toluidin blue for chromidial substance.

OBSERVATIONS

The earliest stages in the succession of morphological events in the corpus luteum in man as it changes from a menstrual to a gravid state are unknown. As no one has as yet had the opportunity of examining these earliest corpora lutea of intra-uterine pregnancy, our knowledge of this vital subject must necessarily be inadequate. But there are sufficient data available about the structure of the menstrual corpus luteum at the

TABLE II.—SIZE OF CORPUS LUTEUM AND OF CENTRAL CAVITY, AND PERCENTAGE OF GRANULOSA-LUTEIN AND THECA-LUTEIN CELLS CONTAINING SECRETORY GRANULES, LIPOID, AND COLLOID DROPLETS IN 19 CASES OF PREGNANCY

Case No.	Age (days)	Size (mm.)	Size of central cavity (mm.)	Granulosa-lutein cells				Theca-lutein cells	
				Secretory granules per cent	Lipoid per cent	Colloid droplets per cent	Cholesterol	Secretory granules per cent	Lipoid per cent
A.—Operative (uterine) cases									
1	c.35	10x 7	Coagulum	50	58	5	Traces	22	44
2	51	18x10	10x 5	40	95	6	Traces	50	47
3	53	22x18	15x10	31	70	15	Traces	26	56
4	63	20x15	15x10	38	41	10		31	51
5	75	20x 9	8x 6	36	23	11		25	22
6	77	18x10	13x 5	45	33	13	Traces	24	26
7	78	19x 9	Loculated	22	35	18	Traces	45	32
8	98	16x 7	5x 2	43	55	15	Traces	40	55
9	127	10x 8	Absent	29	21	11		Absent	Absent
10	135	14x 7	4x 2	16	18	23		29	67
11	280	8x 6	Absent	0.5	10	50		Absent	Absent
12	280	8x 8	Absent	2	9	39 (calcified)		Absent	Absent
13	282	11x 5	Absent	20	7	59		Absent	Absent
B.—Postmortem (uterine) cases									
14	c.110	11x 6	Absent	35	10	Not seen	Traces	25	24
15	c.130	8x 7	Absent	14	6	Not seen		10	37
16	Term	10x 5	Absent	nil	1	Not seen		Absent	Absent
17	Puerperal	6x 4	Absent	2	0.5	11 (calcified)		Absent	Absent
C.—Ectopic cases									
18	47	13x 6	4x 4	17	95	8		27	16
19	c.50	14x12	Coagulum	20	25	9		29	90

height of its activity and that of the corpus luteum in the second month of pregnancy to deduce the probable sequence of events.

After rupture of the mature graafian follicle (corpus folliculare menstruationis of Aschoff) and expulsion of the ovum, the cells of the stratum granulosum, according to most investigators (cf. review of literature by Asdell (1928), enlarge to give rise to the lutein cells.

The site of follicular rupture heals by a proliferation of connective tissue which closes the stigma and converts the whole follicle into the maturing corpus luteum in which a central cavity persists as evidence of the original lumen of the graafian follicle. The corpus luteum grows in size mainly by a hypertrophy of the lutein cells. The mature corpus luteum of menstruation (corpus folliculare efflorescens of Aschoff) is reached 14 days after ovulation when the corpus luteum may measure 18 by 12 millimeters. A hemorrhage now develops, originally in one pole of the lutein tissue (Fig. 1, *A*) and later at several points, finally bursting into the coagulum of the central cavity, and resulting in a central fibrinous clot and obliteration of the cavity (corpus folliculare hæmorrhagicum of Aschoff). Menstruation itself occurs soon after this event. This marks the commencement of the involution of the "menstrual" corpus luteum; connective tissue organization supervenes and the cells become infiltrated with lipoid to produce the characteristic yellow color of the retrogressing corpus luteum (corpus luteum menstruationis of Aschoff). Later the cells degenerate, the lipoid is removed by histiocytes and the scarring

TABLE III.—AREAS OF THE WHOLE GLAND, LUTEIN TISSUE, FIBROUS LAYER AND CAVITY AT DIFFERENT STAGES OF PREGNANCY IN SQUARE CENTIMETERS*

Case No.	Age (days)	Area of cavity (sq. cm.)		Area of fibrous tissue (sq. cm.)		Area of lutein tissue (sq. cm.)		Total area sq. cm. × 625
		Actual × 625	Per cent of total	Actual × 625	Per cent of total	Actual × 625	Per cent of total	
1	c. 35‡							
2	51	242	32	192	25	329	43	763
3	53	414	32	195	15	693	53	1302
4	63	619	51	290	24	316	25	1225
5	75‡							
6	77	146	22	107	16	392	62	645
7	78	13	2	72	11	560	87	645
8	98	27	6	108	22	349	72	484
9	127	0	0	18	6	310	94	328
10	135	11	2	76	12	570	86	657
11	280	0	0	28	15	161	85	189
12	280	0	0	5	2	254	98	259
13	282	0	0	8	2	312	98	320

*Estimated from sections passing through the greatest diameter of the corpus luteum. To obtain the actual area the figures must be divided by 625.
‡Cases 1 and 5 were slightly damaged at operation and are not included since a complete section passing through the middle of the corpus luteum could not be obtained.

process increases. The corpus candicans (corpus folliculare involutum of Aschoff) is thus formed.

In the second month of pregnancy the gland as a whole is larger than the corpus folliculare efflorescens in consequence of the hypertrophy of the lutein cells and an accumulation of straw-colored fluid within the central cavity. The inner rim of connective tissue lining the deepest part of the corpus luteum by that time has increased considerably in thickness (Figs. 2, *D* and 17, *D*).

Instead of the hemorrhage which customarily occurs either immediately before or simultaneously with menstruation, the "pregnant" corpus luteum experiences probably a simple hypertrophy during the period between fertilization and implantation of the ovum.

We have attempted to express in a rough mathematical way the fluctuations in size of the corpus luteum throughout pregnancy. The simple procedure adopted for this purpose was to select the section passing through the greatest diameter of the corpus luteum; the section was projected on graph paper at a magnification of 25 diameters and the whole corpus, the lutein tissue, inner fibrous layer and the central cavity were outlined. The areas were then obtained (Table III) and from this information Figure 3 was constructed. While this method is merely an assessment of relative size in comparing globoid bodies it was the only procedure we could adopt under the circumstances, since the tissue had been cut up according to plan for the specific techniques here mentioned. Nevertheless the results of this procedure reflect with sufficient accuracy for our purpose the progressive growth or diminution of the various parts of the corpus luteum during pregnancy. We have added for purpose of comparison a "menstrual" corpus luteum which was removed one day before the next expected period.

When fertilization occurs the corpus luteum scarcely grows in diameter and volume for the first 50 days of pregnancy (Fig. 3). Between the fiftieth and sixtieth days the corpus luteum doubles its premenstrual area as seen in cross section. By the eightieth day its area in section is once again reduced to that of the premenstrual corpus luteum, and at term has become reduced to half the area presented by the premenstrual corpus luteum and a quarter the area of the "pregnant" corpus luteum at the height of its activity.

The enlargement during early pregnancy is produced chiefly by the formation of the fluid-

containing cavity and the fibrous tissue lining the wall of the cavity which together are responsible for 75 per cent of the increase in size of the corpus luteum. The cavity in one specimen contained as much as 1.75 cubic centimeters of fluid. When the cavity finally becomes very much reduced in size by the eightieth day, the corpus luteum is actually smaller than the premenstrual body.

In one of the intra-uterine cases (Case 1) the central cavity was obliterated by a hemorrhagic coagulum. The lutein cells in this case showed evidence of commencing degeneration; the embryo was dead. Another specimen possessed a cavity which was loculated (Case 7), and no fluid could be withdrawn; in this case the fetus was normal as far as could be ascertained macroscopically, although the placenta was unusually adherent to the uterine wall.

In section (Fig. 2) the central cavity of the corpus luteum in the first 2 to 3 months is lined by a thin smooth rim of edematous white fibrous tissue 1.5 millimeters thick which separates the yellowish lutein wall of glandular cells from the central cavity. The lutein tissue itself forms a folded wall measuring on the average 5 millimeters in thickness.

From the third to the fifth month the corpus luteum decreases in size; this is associated with a gradual obliteration of the central cavity. In the fifth month the cavity is completely obliterated, the fibrous walls of the opposite poles fusing to form a central core of connective tissue and the gland as a whole now measures 12 by 8 by 5 millimeters.

After this period the corpus luteum remains almost stationary in size until term and then diminishes during the puerperium. At birth no trace of the central core of connective tissue is macroscopically visible; the whole gland forms a solid structure.

The lutein tissue generally has a bright orange color in the early stages of pregnancy, while in the latter part of pregnancy it assumes a yellow hue, and at term may be a pale yellow.

MICROSCOPIC APPEARANCE

Under the low power of the microscope the corpus luteum of pregnancy exhibits a false external capsule continuous with the ovarian stroma, but looser in its texture and less cellular. The false capsule contains dilated blood and lymphatic vessels which are especially prominent in the early gravid corpus luteum. In the false capsule of the corpus luteum of the latter half of pregnancy, although the vessels are not so prominent, the walls of the individual vessels are thicker; the increased proliferation of subcapsular connective tissue during retrogression is associated with the absorption of the theca-lutein cells which in turn leads to a recession of the lutein tissue from the blood vessels. The subcapsular blood vessels now lie at a distance from the outer circumference of the corpus luteum.

Lining the central cavity (Figs. 2 and 17) is an inner fibrous connective tissue layer 0.3 to 1.5 millimeters thick, *D*. It is composed of widely separated, young fibroblasts embedded in an apparently edematous matrix of thin, newly formed, collagenous fibers which stain a faint pink with eosin. This tissue thus resembles very closely embryonic connective tissue or mesenchyme. In this layer in some specimens small hemorrhages are seen undergoing organization.

Between the false outer capsule, *A*, and the inner fibrous layer, *D*, the lutein cells are found. Both the false capsule and the inner fibrous layer send trabeculæ or septa into the glandular tissue in such a way that in any given section they interdigitate with each other (Fig. 2). This is responsible for the greatly folded appearance of the lutein tissue seen macroscopically. Although the septa interdigitate in this fashion, a direct communication is found occasionally between the two varieties of septa. Running between the septa are fine reticular fibers forming a scaffolding for glandular cells and fine blood capillaries.

In fortunate sections the remains of the site of rupture of the original graafian follicle may be identified. At this site the granulosa-lutein cells are almost completely absent, so that the theca-lutein cells and capsule come into direct contact with the inner fibrous layer lining the central cavity.

GLANDULAR ELEMENTS

The glandular tissue consists of the granulosa-lutein cells and the theca-lutein cells.

The theca-lutein cells are suspended in a reticular framework which surrounds the regularly clustered cells (Fig. 4, *A*), whereas in the granulosa-lutein tissue the reticulum is impregnated irregularly between the individual cells (Fig. 4, *B*). In the early stages of pregnancy it is characteristic to find the theca-lutein cells in abundance around the large blood vessels in the region of the coarse septa (Fig. 5). In some corpora lutea there may be two to three layers of theca-lutein cells extending between these perivascular accumulations of cells, and thus an almost complete subcapsular rim of theca-lutein cells may surround the gland. As the blood vessels extend from the false capsule to enter the substance of the gland they are ensheathed by masses of theca-lutein cells. Sections cut at right angles to the long axis of these perforating septa display islands of theca-lutein cells which may have no obvious connection with the more peripherally situated elements.

The theca-lutein cells are small polyhedral cells measuring 15 microns on the average. The nucleus of the theca-lutein cell is generally round measuring on the average 7.5 by 6.5 microns, and contains a single, large, prominent, rounded nucleolus. The chromatin is distributed as a large number of concentrations on the linin network, resulting in a nucleus which is usually more hyperchromatic than that of the granulosa-lutein cell. Theca-lutein cells are present until shortly after the fifth month of gestation; there is no evidence whatever of their presence at term. In the early stages they may be very numerous. In one specimen (Case 2), in a cross section through center, the ratio (by area) of theca-lutein to granulosa lutein cells was 8:100.

The granulosa-lutein cells, therefore, form the bulk of the glandular portion of the early corpus luteum and the whole of it in the latter half of pregnancy. The granulosa-lutein cells measure 50 to 60 microns, and are thus three to four times larger in cross section than the theca-lutein cells. The cytoplasm stains less intensely than that of the theca-lutein cell. However, in nearly all cells stained with hematoxylin and eosin the cytoplasm shows a varying degree of affinity for the stain. This staining reaction may attain such a degree of intensity that two types of cells may appear, namely, the "light" and "dark" cells. The pale-staining cells form the majority of cells and are polyhedral or spheroidal in shape; the darker-staining cells tend to be flatter and their margins angular, as if compressed by the adjacent light cells. The nucleus of the granulosa-lutein cell is much larger and more vesicular than that of the theca-lutein cell. It is oval in shape and measures on the average 11.6 by 8.9 microns; it contains one or two, and occasionally even more, prominent oval or rod-shaped nucleoli which are sometimes seen to split or to be extruded into the cytoplasm. The prominent nuclear membrane is delicate, and the chromatin is distributed as fine concentrations on the linin network. In the highly functional, vacuolated cells the nucleus usually shows striking changes; the nuclei become hyperchromatic and sometimes almost pycnotic.

The glandular cells contain specific inclusions, namely: (1) secretory granules, (2) lipoid, (3) colloid droplets, (4) vacuoles, (5) chromidial substance, and (6) mitochondria and Golgi apparatus.

All of these inclusions are found in the granulosa-lutein cells, whereas the theca-lutein cells lack the colloid droplets and vacuoles. The relative percentages of glandular cells encountered containing secretory granules, lipoid and colloid droplets have been estimated for the luteal tissue in each of our cases and are detailed in Table II, and represented graphically in Figure 6. The Golgi apparatus and mitochondria and the changes they undergo will be described in a separate study.

1. Secretory granules are well demonstrated by Mallory's connective tissue stain, which colors them a deep red against the blue cytoplasmic background. In the granulosa-lutein cells (Fig. 7) they occur as fine, red granules or even as rodlets varying from a few up to 60 or more per cell and measure 0.5 to 1.2 microns. These granules may be scattered throughout the cytoplasm, but they frequently aggregate and become localized to one pole of the nucleus. Sometimes they are arranged in a row occupying the peripheral cytoplasm, the intervening cytoplasm being

free from granules. Cells containing granules possess a well formed, oval, vesicular nucleus; vacuoles, as will be noted, are rarely to be seen, and, if found, are small in size. The granule-containing cells occur most abundantly in the middle and peripheral zones of the lutein wall and are much less numerous in those granulosa-lutein cells which occupy the inner zone where the most highly vacuolated cells are present.

In the theca-lutein cell the granules are slightly larger measuring up to 2 microns and only a few occur in an individual cell (Fig. 8), but the percentage of cells containing granules may be as numerous as we discover among the granulosa-lutein cells (see Table II).

The percentage of cells containing secretory granules forms a fairly reliable index of the age of the gravid corpus luteum (Table II). Granules are most numerous during the first half of pregnancy when they occur in approximately over 30 per cent of the cells; at the end of pregnancy only 2 per cent or less of cells contain granules. In one specimen at term, however, 20 per cent of cells still contained secretory granules (Case 13).

2. *Lipoid* occurs in the granulosa-lutein cells in the form of very fine droplets, which are numerous in the individual cell and frequently form a peripheral cytoplasmic zone (Fig. 9). Occasionally, however, the droplets increase progressively in size until finally the whole cell may stain a bright orange-red color in scharlach R—hematoxylin stained frozen sections with the blue-stained nucleus lying in the center. In such a cell the individual droplets still remain discrete (Fig. 10, *A*). Such cells may show the presence of anisotropic lipoid (Figs. 11 and 12) or cholesterol by the Schultz test (Fig. 13). One to five of these lipoid masses may be seen per low power field (×80); their presence as isolated cells among the granulosa-lutein cells in the corpus luteum makes a picture which is characteristic of the early part of pregnancy. They are not seen in the corpus luteum of the latter half of pregnancy.

Very few of these fat droplets are blackened by osmium tetroxide in frozen sections. The majority show no blackening at all or only a slight grayish brown tinge. After Bensley's osmic-bichromate-acetic mixture the lutein cells in paraffin sections contain large numbers of blackened lipoid which is almost identical in distribution with that of the scharlach R stained frozen sections.

In the highly vacuolated cells fine, lipoid droplets are very rarely present. In these cells larger droplets do occur and occasionally the vacuoles themselves take up the scharlach R with the result that a large, red-staining blob is seen, which may appear, like the vacuole, to lie extracellularly. These large blobs of fat, however, are not very common; they are entirely different from the conglomerate mass of discrete, lipoid globules described. The globules in these vacuolated cells and in the vacuoles themselves are more easily blackened with osmium tetroxide, so that in some cases a rim of cells with blackened lipoid is seen in the innermost two or three layers of granulosa-lutein cells adjacent to the fibrous layer.

In the theca-lutein cells the lipoid droplets are relatively larger and few are found in each cell. They are for the most part not blackened with osmium tetroxide.

The granulosa-lutein cells show a distinctly progressive decrease in the percentage of lipoid-containing cells during pregnancy, dropping from 50 per cent and over in the early part of pregnancy to 10 per cent and under at term, whereas the theca-lutein cells are variable in this respect (Table II).

Traces of anisotropic lipoid, which gave the Schultz positive test for cholesterol, were found in the granulosa-lutein cells of only 7 cases. The almost complete absence of visible cholesterol is a noteworthy feature of the corpus luteum throughout pregnancy.

3. *Colloid droplets* are present only in the granulosa-lutein cells and are absent from the theca-lutein cells. In the first 2 months of pregnancy they occur in under 15 per cent of cells, whereas at term 50 per cent of cells may contain colloid (Fig. 16). In the early cases they measure 3 to 10 microns and only one or two droplets occur in the cell. In the later specimens, however, they increase in size to form larger droplets and at the same time they also accumulate in greater numbers in the individual cell. In some cases the increase in

size is due to fusion of the droplets. Finally the cell may disintegrate leaving a colloid mass not surrounded by any recognizable cytoplasm so that the colloid appears to lie extracellularly.

With Mallory's connective tissue stain the colloid droplets may stain either red, blue, or yellow. With hematoxylin and eosin they generally stain a pale pink color, but in two instances (Cases 12 and 17) they showed a marked affinity for the hematoxylin, staining a distinct blue and suggesting the possibility of calcification (Fig. 14).

Colloid droplets are apparently very labile and are not found unless the specimen is fresh. Thus they were absent from the autopsy specimens except for the one case in which they had become calcified.

The colloid droplets develop within the vacuoles, and all stages may be seen from the vacuole to the fully formed colloid droplet. The peripheral rim first stains and later the whole vacuole (Fig. 15). At first the colloid stains a pale blue or yellow with Mallory's stain; in this phase it may be reconverted into colorless secretion so that clear vacuoles appear within the stained colloid mass giving the whole a fenestrated appearance. If, however, the colloid stagnates within the cell it becomes a dense, spherical mass which is colored a deep red with Mallory's stain. In the later course of pregnancy these dense spheres may become calcified (Fig. 14).

4. Vacuoles occur in the cells as colorless, round spaces in the cytoplasm of the granulosa-lutein cells. Like the colloid droplets they are absent from the theca-lutein cells.

In the early stages of pregnancy the cells containing vacuoles are exceedingly numerous, and, under low power, especially in the neighborhood of the central cavity, the sections have a moth-eaten appearance. Vacuoles may occur in any of the granulosa-lutein cells; but the cells occupying the inner third of the lutein wall adjacent to the fibrous lining of the central cavity are the most highly vacuolated (Fig. 17, *C*) and are obviously participating in an active secretory process.

The vacuoles first make their appearance in the cytoplasm as small, nonstaining, circular areas which gradually enlarge and fuse so that the whole cell becomes filled with a large vacuole surrounded by a thin rim of cytoplasm. The nucleus is frequently pushed to the periphery and becomes wrinkled and hyperchromatic and even pycnotic. Where several cells lying together show such large vacuoles they resemble a gland-like acinus.

Specimens from the latter half of pregnancy contain fewer vacuoles in contrast to the earlier actively secreting gland. The contents of the vacuoles have become progressively stainable and form the colloid droplets, which accounts for the progressive increase in the number of colloid-containing cells toward term.

5. Chromidial substance occurs as numerous filaments and triangular or club-shaped bodies in the cytoplasm of the granulosa- and theca-lutein cells. Owing to their great diversity in size and shape it was not possible to make a quantitative estimation of the relative number of cells containing this substance; they are most numerous in the early months and decrease greatly in quantity in the later months of pregnancy.

COMMENT ON MACROSCOPIC APPEARANCE OF THE GRAVID CORPUS LUTEUM

The most remarkable feature of the corpus luteum of early human pregnancy is the development of a relatively huge fluid containing cavity within the center of the gland.

The cystic corpus luteum has been described thus far in only a few pregnant mammals. It was noted in the ovary of a pregnant gorilla (Saglik, 1938). Van der Stricht (1912) also described a transient cavity in the corpus luteum of the bat. Rabl (1899) first drew attention to the fluid-filled cavity in the human corpus luteum of pregnancy. This was confirmed later by Seitz (1906) and Marcotty (1914).

With the exception of Shaw (1936) the cystic character of the corpus luteum is not described in English textbooks of gynecology and obstetrics. German textbooks, however, pay attention to this phenomenon (Aschoff, 1924, and Schroeder, 1930).

The early increase in size of the corpus luteum is largely accounted for by the growth of the cavity and the accumulation of fluid. This is obvious from Table II where, in Cases 3 and

Fig. 1. Photomicrograph of a section through a corpus luteum removed 1 day before next expected menstruation. Note blood clot at one pole, *A*, and remains of cavity of original graafian follicle. Hematoxylin and eosin, ×3.3.

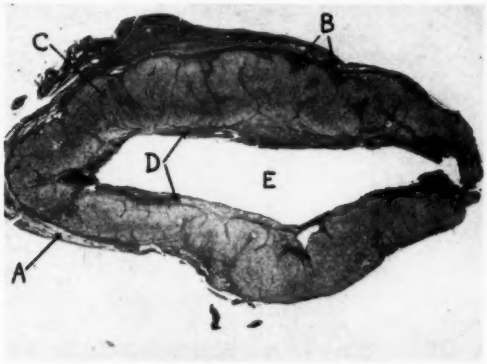


Fig. 2. Photomicrograph of a section through a corpus luteum of a 77 day pregnancy (Case 6). *A*, capsule; *B*, theca-lutein cells; *C*, granulosa-lutein cells; *D*, inner fibrous layer; *E*, central cavity. Hematoxylin and eosin, ×3.3.

4, the cavity in a section through the largest diameter represents by area one-half of the corpus luteum. Further, when the cavity becomes smaller there is a diminution in size of the corpus luteum as a whole. The cavity reaches its maximum size, according to our observations, between the fiftieth and sixtieth days. Thereafter it diminishes in size becoming a tiny space (Case 10), or completely obliterated (Case 9) at about the fifth month. It is entirely absent at term.

Seitz, who made accurate measurements of human corpora lutea of pregnancy, found that the corpus luteum reached its maximum size in the second to third month when it measured 1.8–2 by 2–2.5 centimeters. This observation we are able to confirm (Table II). After the fifth month, according to Seitz, the corpus luteum becomes smaller although a slit-like space was present at the seventh month in one of his cases. Marcotty recorded the absence of the cavity after the sixth month.

On account of individual variations in size of the corpus luteum during pregnancy Seitz could not construct a growth curve from his material. Despite the limited number of corpora lutea associated with intra-uterine pregnancy it is important to essay such a growth

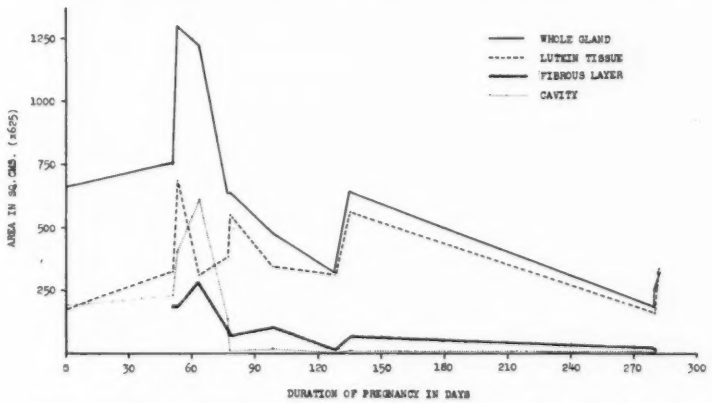


Fig. 3. Graph showing area of whole gland, lutein tissue, fibrous layer and cavity at different stages of pregnancy. From data given in Table III.

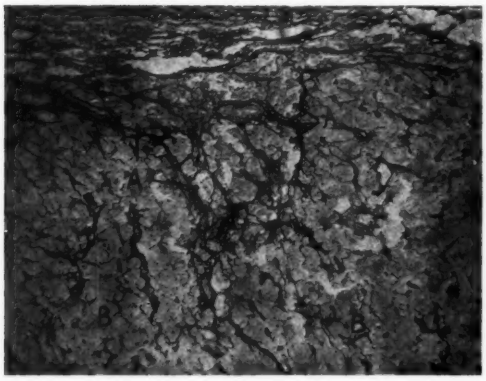


Fig. 4. Low power photomicrograph showing distribution of reticulum. Bielschowsky-Foot silver method counterstained with neutral red, ×97. *A*, theca-lutein cells grouped in clusters by the reticulum; *B*, granulosa-lutein cells with reticulum running irregularly between them.

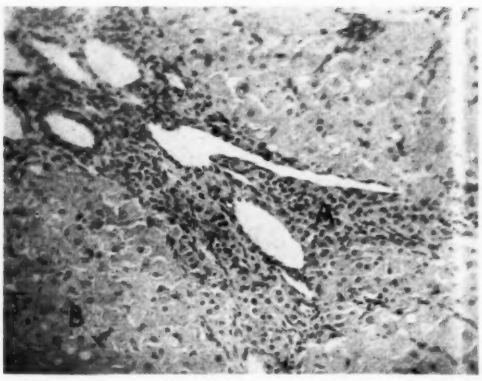


Fig. 5. Low power photomicrograph to show general arrangement of theca-lutein cells. *A*, round blood vessels, and granulosa-lutein cells, B. Hematoxylin and eosin, ×97.

curve of the corpus luteum of pregnancy (Fig. 3) if only to form a basis upon which more comprehensive statistical examinations of the growth of the corpus luteum throughout pregnancy can be constructed.

The corpus luteum rapidly increases in size after the fiftieth day of pregnancy. This is maintained until the sixtieth day when it rapidly diminishes in size. The diminution is due to an obliteration of the central cavity and a diminution in thickness of the fibrous tissue immediately surrounding the cavity. The lutein tissue remains fairly constant in volume throughout pregnancy.

COMMENT ON MICROSCOPIC APPEARANCE OF THE GRAVID CORPUS LUTEUM

Granulosa-lutein and theca-lutein cells. The two component elements of the human corpus luteum have been known since the beginning of the present century (Pinto, 1905). There is now unanimity of opinion as to the existence of the two cellular entities but controversy still rages as to their origin (Asdell, 1928). The bulk of evidence is in favor of a separate origin of the theca-lutein and granulosa-lutein cells, the former from the theca interna and the latter from the stratum granulosum of the graafian follicle. We agree with this view;

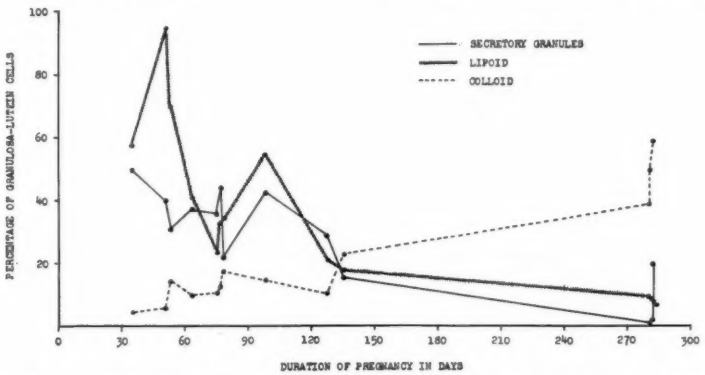


Fig. 6. Graph showing percentage of granulosa-lutein cells containing secretory granules, lipoid, and colloid at different stages of pregnancy. From the data recorded for 13 intra-uterine cases in Table II.

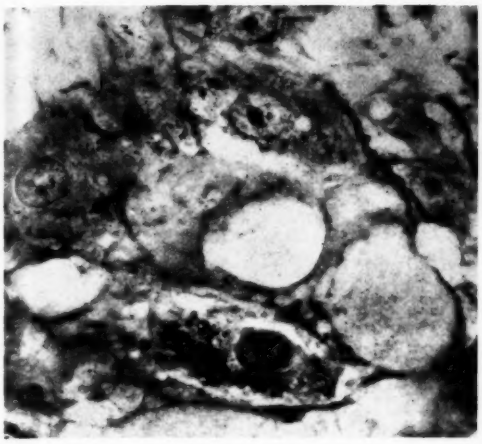


Fig. 7. Oil immersion photomicrograph showing secretory granules in granulosa-lutein cells. Mallory's stain, ×1345.

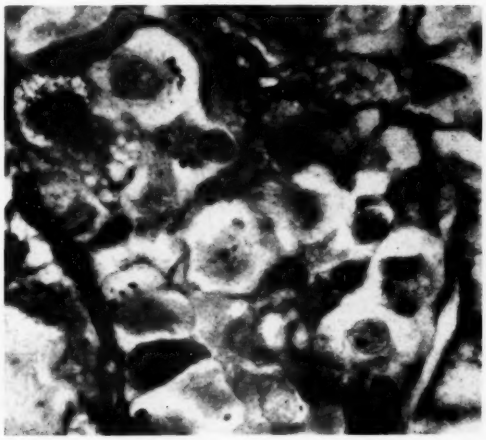


Fig. 8. Oil immersion photomicrograph showing secretory granules in theca-lutein cells. Mallory's stain, ×1345.

theca-lutein cells have not been found to metamorphose into the granulosa-lutein cells.

The theca-lutein cells are very prominent in the early months of pregnancy. In a single section passing through the center of the corpus luteum we find that thecal cells form as much as 8 per cent of the total area of the lutein tissue. As pregnancy advances the theca-lutein cells diminish in number until after the fifth month; then they disappear completely. In this respect the theca-lutein cells in the corpus luteum approximately parallel the growth and atrophy of the luteal cavity.

It is advantageous to mention here that a rhythmic formation and atresia of graafian follicles proceeds in the ovary throughout pregnancy. In the atretic follicles the theca interna cells enlarge and replace all other cellular elements. The degree of thecal cell-activity is generally more intense than occurs in atretic follicles encountered in the ovary during the menstrual cycle. The enlarged thecal cells in atretic follicles during pregnancy are indistinguishable structurally from the theca-lutein cells of the young gravid corpus luteum. Long after the theca-lutein cells have disappeared from the gravid corpus luteum, enlarged thecal cells are still to be found in these atretic follicles.

The granulosa-lutein cells are the typical glandular elements of the corpus luteum. Their general structure is sufficiently well known not to merit further description. One feature, however, needs more careful examination.

Some investigators have suggested that the darkly-staining and lightly-staining cells, which normally occur in the gravid corpus luteum, are indeed two distinct cell types. Corner (1919) has even described a third type in the pregnant sow.

Dark and light cells are present in every organ whether exocrine or endocrine. The nature of the dark cell in different glands may vary. Thus in the suprarenal and parathyroid the dark cells are known to be storage phases which ultimately degenerate in a large percentage of cases. In the goblet cell of the bowel and trachea they were found to be exhausted cells (Gillman, 1939).

In the corpora lutea from ectopic pregnancies in which fetal death had occurred, the proportion of dark cells is recognizably increased. The evidence from other tissues suggests that the dark and light cells in the corpus luteum merely represent different phases of secretory activity in the granulosa-lutein cells. As in other organs, many of the dark luteal cells ultimately degenerate.

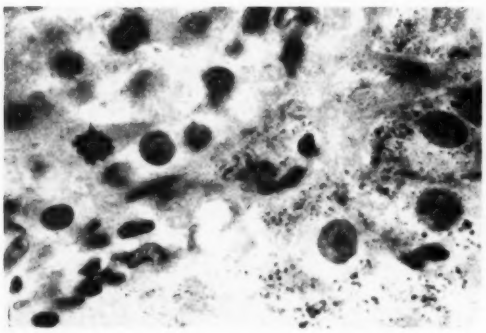


Fig. 9. Oil immersion photomicrograph to show fat droplets in the granulosa-lutein cells. No lipoid is seen in the theca-lutein cells in this region; one theca-lutein cell shows a mitotic figure. Frozen section. Scharlach R and hematoxylin, ×980.

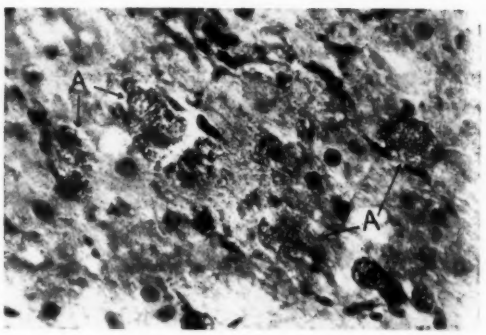


Fig. 10. Photomicrograph showing scattered granulosa-lutein cells laden with discrete lipoid droplets, *A*, which stain a bright red with scharlach R and are frequently anisotropic (see Figures 11 and 12). Frozen section, scharlach R and hematoxylin, ×315.

Nucleus. Khvatov (1938) claimed that the nuclear size of the lutein cell in the rabbit tends to increase during pregnancy. We have measured one hundred nuclei in each of 3 cases, at the beginning, middle, and the end of pregnancy. The average size of the nucleus (and the standard deviation) was as follows: Case 4, 63 days, 11.8 ± 1.3 μ; Case 10, 135 days, 12.1 ± 2.5 μ; Case 11, 280 days, 10.9 ± 2.3 μ. There is thus no correlation in man between nuclear size and the length of gestation.

Secretory granules. As far as we can ascertain from the available literature the red-tinted granules seen in the theca-lutein and granulosa-lutein cells, after staining with Mallory's connective tissue stain, have not been described in the human corpus luteum. These granules are not specific for pregnancy, as they have been observed in corpora 2 or 3 days before the onset of menstruation. They occur especially in the early months of pregnancy where 50 per cent of the cells contain some granules, and gradually diminish until toward the end of gestation when only 2 per cent are granulated cells.

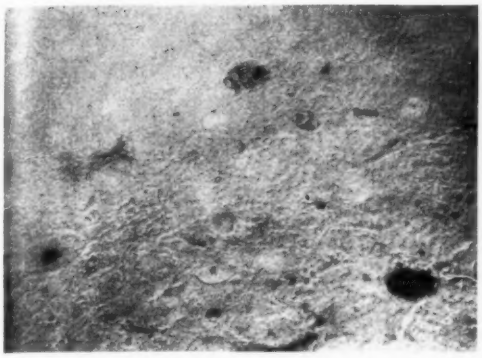
Drips (1919) using the Altmann technique for mitochondria found granules in the corpus luteum of the spermophile in the early stages of pregnancy. On account of the technique used by her it is not clear to us whether these granules in the spermophile are mitochondria, secretory granules, fat, or a mixture of the three. Drips states that in the late stages of pregnancy lipoid droplets appear which become abundant at birth. Following perhaps the lead given by Van der Stricht in his study of the bat, she believes the secretion of the lutein cells to be serous in the first half of pregnancy and lipoidal in the second half.

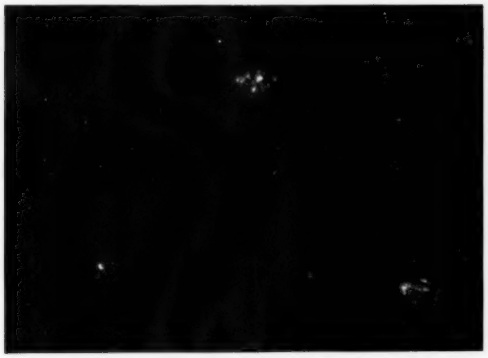
The secretory granules in the human corpus luteum are almost entirely absent from cells containing big vacuoles or colloid droplets. It has not been possible to establish the fate of these granules, but they may be the precursors of the nonstainable secretion in the vacuoles of the highly active cells. We have not been able to demonstrate with confidence their transformation into such secretion. They certainly do not give rise directly to the colloid droplets.

Lipoid. Meyer (1911) first described the presence of lipoid in the corpus luteum of pregnancy. Miller (1914) who considered all "fat" to be neutral fat, found no evidence of its existence in the gravid corpus luteum except during the puerperium.

Owing to technical difficulties existing at that time these observations are not entirely free from criticism. Meyer used the Sudan staining method on paraffin sections, while Miller regarded the Sudan staining without preliminary chroming as a technique for demonstrating neutral fat only and not for lipoid.

Marcotty (1914) appears to have been the first to use methods which are approved as





Figs. 11 and 12. Photomicrographs of the same scharlach R stained section in ordinary light and under polarized light (crossed Nicol's prisms) to show anisotropic lipoid. ×315.

techniques for the identification of lipoid, namely, Sudan III and polarized light applied to frozen sections, in addition to the now discarded Nile-blue-sulphate method. He found that young corpora lutea contained much fat in the theca-lutein cells and less in the granulosa-lutein cells. Later in pregnancy this distribution is reversed and the granulosa-lutein cells then contain more fat than in the early months. From the third to the seventh month very little fat is present. After the eighth month, however, the fat reaction becomes marked and this is further intensified during the puerperium. Some of these fat droplets according to Marcotty, were anisotropic under the crossed Nicol's prisms; he mentions the presence of such doubly refractile bodies in the early specimens, but not for the later specimens.

Moulonguet-Doleris (1925) found fat to be present only very early in pregnancy, diminishing considerably after the second month. He, therefore, considered that the gland functioned only early in pregnancy. He regarded the fat staining of sufficient significance to distinguish between the corpus luteum of pregnancy and that of menstruation. The fat in the gravid corpus luteum is labile being inconsistently soluble in xylol after osmication; the major part of it was anisotropic; and it formed characteristic pools or lakes, showing a diffuse impregnation with the fat stains. That of the menstrual corpus luteum however was stable, isotropic, and occurred as fine droplets.

There is thus in the literature considerable uncertainty as to the qualitative and quantitative distribution of luteal cellular fat at the various stages of pregnancy. Our own observations indicate that the number of fat-containing cells is much greater at the beginning than at the end of pregnancy (Table II), and that fat is found at least in some cells throughout the entire course of pregnancy. The fat generally occurs as fine droplets; these may later fuse and give rise to large globules. The accumulation of large discrete lipoid droplets in isolated granulosa-lutein cells (1 to 5

Fig. 13. Photomicrograph of another frozen section from the same case as Figures 11 and 12. Treated by the Schultz method to show the greenish-blue deposits of cholesterol appearing black in the photograph. ×358.

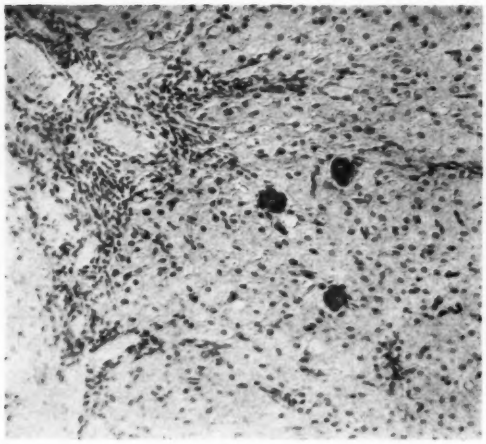


Fig. 14. Low power photomicrograph to show absence of theca-lutein cells and calcification of colloid at term (Case 12). Hematoxylin and eosin, ×125.

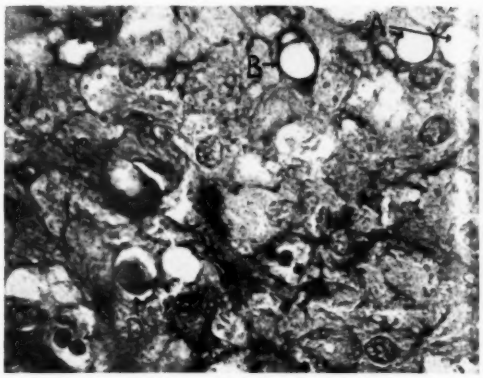


Fig. 15. High power photomicrograph to show the evolution of the colloid droplet from the nonstaining secretion in vacuoles. From a case 98 days pregnant (Case 8). Mallory's stain, ×475. *A*, nonstaining vacuoles; *B*, peripheral staining of vacuole to form colloid; *C*, colloid with vacuole in it; *D*, fully formed colloid.

per low power field) is characteristic of the corpus luteum of early pregnancy. Such cells are apparently similar to the granulosa-lutein cells of the involuting menstrual corpus luteum; in the latter, however, the whole gland is composed of these lipoid-laden cells. In the gravid corpus luteum the lipoid of these isolated cells is also frequently anisotropic and Schultz positive for cholesterol; thus cholesterol was detected only as traces in 7 of our cases in the granulosa-lutein cells of the first 5 months of pregnancy. The relative absence of cholesterol throughout pregnancy is characteristic of the gravid corpus luteum; the impression given by textbooks that the corpus luteum, next to the adrenal, is the greatest site of cholesterol deposition is based on the examination of corpora lutea undergoing retrogression during the menstrual cycle. Visible cholesterol is not found to any extent in the actively functioning corpus luteum of pregnancy and the traces that are found probably represent a degenerative phenomenon of highly active, granulosa-lutein cells, which have failed to recover at the end-stage of the secretory cycle.

Colloid droplets, calcium and vacuoles. Colloid droplets in the corpus luteum of pregnancy were first described by Rabl (1899) and later by Pinto (1905) and Seitz (1906). Miller (1914) found them to be present in 22 of 28 cases and was the first to draw attention to their value as a criterion diagnostic of the corpus luteum of pregnancy. According to Miller their quantity showed no relationship to the duration of pregnancy, the largest amounts were found in 2 cases of the first and third months and in a case during the puerperium.

Miller, cited by Marcotty, was also the first to draw attention to the fact that calcified droplets were frequent in the pregnant corpus luteum, having found them in all his cases, with the exception of one, in the second half of pregnancy.

Marcotty (1914) never saw colloid droplets in the corpus luteum of menstruation, whereas he found them in nearly every case of pregnancy. On analyzing the protocols submitted by Marcotty we noticed that those cases of corpora lutea of pregnancy which he stated contained no colloid were autopsy specimens. Our observations show that the colloid is very labile and is very susceptible to postmortem autolysis. Colloid droplets are described by Marcotty as being most abundant in the first to third months, diminishing in the latter half of pregnancy.

Marcotty described calcified bodies in 6 corpora lutea toward the end of pregnancy and in 2 during the puerperium.

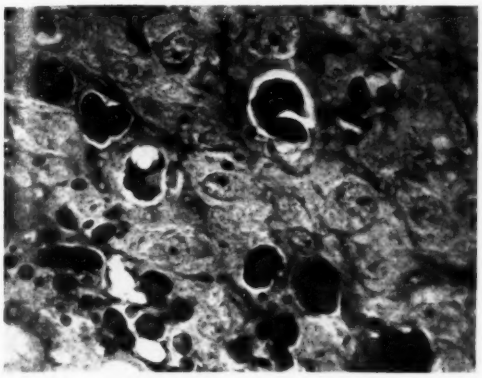


Fig. 16. High power photomicrograph to show excessive amount and nature of colloid occurring in the corpus luteum at term (Case 11). Mallory's stain, ×475.

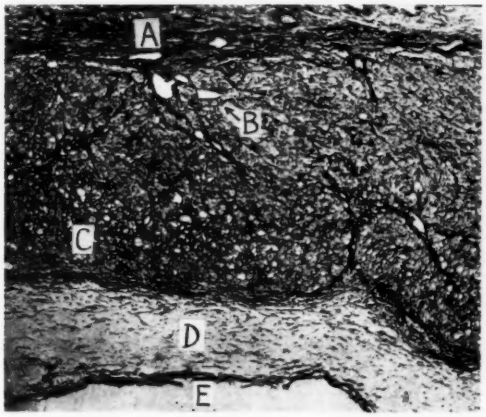


Fig. 17. Low power photomicrograph to show the marked vacuolation of the granulosa-lutein cells occupying the inner third of the lutein wall in early pregnancy (Case 4). Mallory's connective tissue stain, ×38. *A*, capsule; *B*, theca-lutein cells; *C*, vacuolated granulosa-lutein cells; *D*, inner fibrous layer; *E*, central cavity.

Portes, Aschheim, and Robey (1938) found colloid droplets in every case of pregnancy, but never in the "menstrual" corpus luteum, and they suggested that this fact may be used as medicolegal evidence for the diagnosis of pregnancy. They regarded the colloid droplets as evidence of an active secretory process because (a) no accompanying cellular degeneration (lysis and pycnosis of nuclei) was seen within the cells where colloid droplets are found; (b) it appeared in the early gravid corpus luteum, which was undergoing marked functional activity and its presence was indispensable for maintaining gestation; and (c) they are not more abundant at term and during the puerperium than in the early months of pregnancy.

We are unable to accept this suggestion as we have found a quantitative increase throughout the course of pregnancy (Table II) and all the cytological evidence available strongly suggests that the cells containing big colloid droplets are inactive and many are even degenerated. We are led to conclude that the colloid droplets represent a stagnation of the secretion which, in the early cases, appears as nonstainable vacuoles in the cell. The calcified bodies are in our opinion merely a further stage of degeneration of the stagnant colloid droplets.

We may represent the sequence of events involved in the evolution of the colloid droplets as follows:

Vacuoles (non stainable secretion of highly active cell)	⟷	Colloid droplets (stainable secretion tending to stagnate in the less active cell)	→	Calcium bodies (calcification of the colloid droplets = degeneration)

The colloid droplets are probably not completely degenerative secretory products except when they become calcified, and it is possible that the less dense, colloid droplets may be absorbed by becoming reconverted into the nonstainable substances seen in the phase of vacuolar formation. The value of the colloid as a medicolegal test, as suggested by Portes, Aschheim and Robey, is lessened when one considers that it is so labile to postmortem changes, except when calcified.

Since the time that Miller first described colloid droplets in the pregnant corpus luteum, it has always been regarded as characteristic of pregnancy. Colloid droplets have never been seen in the "menstrual" corpus luteum. One of our cases of a corpus luteum removed at the height of activity on the day prior to the next expected menstruation showed the presence of colloid droplets in 0.75 per cent of cells. The possibility still exists that this corpus luteum may have been associated with a very early pregnancy. If this should not be the case then the most reliable

diagnostic criterion is still the increased number of colloid containing cells, since the lowest percentage recorded for our early pregnant corpora lutea was 6 per cent (Table II) whereas in this case there were only 0.75 per cent of colloid containing cells. In the postmortem specimens, however, on account of the greater lability of the colloid even this quantitative test is of little value.

THE FUNCTION OF THE CORPUS LUTEUM OF PREGNANCY

The function of the corpus luteum of pregnancy has been investigated mainly by adopting two methods: experimental and histological.

Excision of the corpus luteum. Largely as a result of the classical experiments of Fraenkel on rabbits in the early part of the century, the opinion became established that the corpus luteum is indispensable for the maintenance of pregnancy. As more and more different species of animals were used for experiments it transpired that, whereas in some animals the corpus luteum was necessary throughout gestation, in others it could be removed at some period without interfering with the pregnancy.

Removal of the corpus luteum causes abortion in the squirrel (Drips, 1919) and in the goat (Drummond-Robinson and Asdell, 1926). Corner (1928) showed that, when bilateral oophorectomy is performed in the rabbit 14 to 18 hours after mating (4 to 8 hours after ovulation), ova develop to the blastocyst stage, but the uterus does not undergo progestational proliferation and the embryo consequently dies. It is common knowledge that, in the rabbit, castration after the twentieth day is not necessarily followed by abortion. Robson (1937) found that abortion occurs in hypophysectomized pregnant rabbits however, if progesterone is administered to such animals, the pregnancy is not terminated.

On the other hand in the mouse the presence of corpora lutea is essential throughout pregnancy (Parkes, 1928). Castration before the fifteenth to sixteenth day leads to absorption of the embryo; after the fifteenth to sixteenth day abortion is precipitated with an unusually high percentage of stillbirths (Harris, 1927).

In pregnant guinea-pigs Herrick (1928) discovered that castration at various periods caused abortion in the majority of his animals (15 of 18), but it was possible for pregnancy to continue if the ovaries are removed even before the middle of the gestation period.

Bilateral oophorectomy in the pregnant mare on the two hundredth day also does not necessarily interrupt the pregnancy, as a foal was born on the three hundred and forty-seventh day (Hart and Cole, 1934).

Courrier and Gros (1935) observed that, in the cat with a normal gestation period of 64 days, abortion did not occur if the castration was performed after the forty-ninth day. Implantation occurs on the thirteenth day and if oophorectomy is practiced between the fifteenth and forty-fifth day pregnancy is always terminated.

The recent work of Hartman (1939) shows that excision of the corpus luteum of the pregnant monkey even on the thirty-first day of gestation did not produce abortion.

In the human female removal of the corpus luteum during pregnancy has been practiced. Simmonet and Robey (1939) have reviewed some of the available literature on this subject. These are set out in Table IV.

TABLE IV[1]

Author	Year	No. of Cases	Duration of pregnancy	Abortions
Peuch and Vanverts	1913	20	First 2 months	Nil
Ask-Upmark[2]	1926	51	First 2 months	1
Pratt	1927	2	20th and 31st days	Nil
Waldstein	1929	1	34th day	Nil
Macias y Torres	1933	2	40th and 46th days	Nil
Brouha and Kricdelka	1934	1	32–38th day	Nil
Brindeau and Hinglais	1934	1	Second month	Nil

[1] From Simmonet and Robey, 1939.
[2] According to an abstract in J. Obst. & Gynaec. Brit. Emp., 1927, 34: 461, and Jones and Weil, 1938, there were 17 abortions and not one as recorded by Simmonet and Robey.

Douglass (1931) reported the persistence of pregnancy after excision of the corpus luteum 4 weeks after the last menstrual period, while Corbet (1932) reported a similar result in a pregnancy of 42 days' duration. Later Jones and Weil (1938) described a case going on to term despite the excision of the corpus luteum on the fifty-eighth day of pregnancy.

On the other hand De Lee (1916) reported 2 cases and Wilson (1937) 5 cases in whom excision of the corpus luteum resulted in abortion.

Asdell (1928) collected 34 cases from the literature in whom bilateral ovariectomy was performed from the first to the seventh month of gestation and found that only 4 aborted. Asdell points out, however, that only those cases which oppose the view that oophorectomy produces abortion have been considered sufficiently interesting to warrant publication.

Despite this objection raised by Asdell there are sufficient cases on record to indicate that removal of the corpus luteum in the human female does not necessarily precipitate abortion. Obstetrical literature reveals that there has been a growing acceptance of the fact that removal of the corpus luteum in the second half of pregnancy is unlikely to interfere with gestation, but it now appears as if the removal of the corpus luteum very early in pregnancy also may not affect the normal progress of the pregnancy.

Histological. The histological approach to the elucidation of the function of the corpus luteum has not proved very attractive to investigators. The general attitude up to the present has been that the corpus luteum of pregnancy is merely a more active corpus luteum than that encountered normally in the second part of the menstrual cycle, that it increases for a variable period in the early stages of pregnancy and then involutes and disappears. These views find expression in most textbooks on obstetrics.

From a review of the data set forth in the body of this paper the central feature that emerges is the extreme activity of the corpus luteum in the first and second months of gestation; the corpus luteum then reaches its maximum size, the percentage of cells containing the secretory granules and lipoid is maximal, and colloid is present in only a small percentage of cells (Table I and Fig. 6). After that period there is a fairly rapid decline in all those features which are usually encountered in an active gland. One peculiarity of the early corpus luteum of pregnancy has particularly impressed us, namely, the development of the cystic cavity filled with what must be regarded as a very potent hormone-containing fluid (Gillman and Smyth, 1939).

This cavity is enclosed not by epithelium or blood vessels, but, on the contrary, by a thick wall of seemingly edematous, fibrous tissue. This structure of the cyst wall is enigmatic; since, if the fluid were required by the organism, it is peculiar that such a strong wall should have been thrown down around a much needed secretion. Nowhere else in the whole body is there to be found a mechanism of this type elaborated for facilitating absorption! We know from what obtains in other endocrine glands that the absorbing cells are in most intimate contact with the circulation. The general cytological arrangements in other endocrine glands are such as would appear likely to facilitate the transport of secretion directly from the cells or fluid-containing cavities into the circulation.

In the corpus luteum on the other hand this very active secretion is walled off, so to speak, from the general circulation.

An important point in solving this riddle is the appearance in time of the potent hormonal fluid and the fibrous tissue around it. Is the dense fibrous layer present before the accumulation of fluid reaches a maximum, or is it laid down only after the maximal production of fluid has been reached?

If, for argument's sake, we accept the former view we must indeed wonder why nature has placed such an efficient barrier in the way of the passage of secretion to the central cavity. The cavity is largest when secretory granules, lipoid droplets, and nonstainable vacuoles are maximal and colloid droplets minimal; it disappears at the fifth month when the ratio of these inclusions becomes reversed. On this hypothesis secretory activity necessarily takes place across a barrier of fibrous tissue and we would therefore have to interpret the function of the corpus luteum as follows:

secretory activity in ascendancy	to 60th day	secretory activity declining	to 130th day	involution	to term

If, however, we take the alternative view that the fibrous tissue is laid down only after the maximal production of fluid has been reached, and that the function of the fibrous

tissue is to wall off a surplus of secretion which is not required by the organism, then we would have to interpret the function of the corpus luteum as follows:

secretory activity in ascendancy and secretory activity in decline	to 60th day	involution	to term

What is the state of the lutein cells in such corpora lutea as contain abundant luteal fluid? The histological criteria point to their being in a state of great functional activity as evidenced by the numerous secretory granules, the huge nonstainable vacuoles in the cell, the massive quantities of fine lipoid and also by the state of the Golgi apparatus which is so huge as to be unparalleled in size by any other Golgi apparatus including even the motor nerve cell. Even though these cells are obviously in the throes of great secretory activity, a large quantity of secretion is accumulating in the cells as nonstainable substances in the form of vacuoles and later as the stainable colloid droplets, the latter increasing progressively in size and numbers. It is clear that the stimulus for elaborating secretion is being continually applied in the early weeks of pregnancy and that the cells are responding in an excessive manner. Whether any of this secretion is poured directly from the cells into the circulation is difficult to say, but there is abundant evidence that quite a considerable amount of the secretion is being stacked up in the cells.

There are two processes in the secretory cycle of the glandular cells: the first is the elaboration of the secretion by the cell and the second is the discharge of the secretion from the cell. These processes must be dependent upon two different and antagonistic or synergic stimuli, for we know that cells can form their secretion but are unable to discharge it until the appropriate stimulus is applied; this is seen for example in the acinar cell of the pancreas, where the zymogen granules may crowd the cell but are only discharged when required.

In some endocrine glands, the thyroid for example, the discharged secretion may be stored for some period in follicles lined by epithelium. These follicles are big or small and the size of the follicles depends upon two factors, namely, the rate of formation and the rate of absorption of the secretion. If the thyroid epithelium is forming its secretion and discharging it, as is generally thought, into the follicle, and if the absorption is proceeding at the same rate as its formation, then clearly there will be no increase in the size of the follicle. If, however, the secretion is being formed at a much greater rate than it is being absorbed, then obviously the thyroid follicle increases in size. The formation of cysts in the thyroid and pituitary as well as in other endocrine glands seems largely dependent on these two factors.

If we apply to the corpus luteum around the fiftieth to sixtieth day interval of pregnancy the principles which seem to apply to endocrine glands like the thyroid and the pituitary, we see that the lutein cells are highly active; they are obviously forming the secretion which is accumulating in the cells in the form of vacuoles and even of less easily absorbable colloid. Some of this secretion may be poured into the circulation, but a great deal of the secretion is also accumulating in the central cavity where it becomes walled off by a layer of connective tissue, which either excludes the secretion from the circulation, or allows it to enter only very slowly. In short the secretion is unnecessary to the organism at the fiftieth to sixtieth day. This circumstance appears to us to explain the accumulation of the fluid and the development of its surrounding fibrous wall.

The conclusion we have drawn, therefore, from the histological features of the corpus luteum is that the luteal secretion poured into the central cavity is probably not required (from between the fiftieth and sixtieth days) in the quantity it is elaborated.

Excision experiments in the human female and in monkeys show that, at least in a large number of well authenticated cases, the corpus luteum is not really essential even in the early phases (50 to 60 days) of pregnancy. The histological appearance of the early gravid corpus luteum in our own opinion corroborates the conclusion which might be based on those experimental findings.

The "critical" period during pregnancy. The structure of the corpus luteum undergoes

important modifications from the fiftieth to eightieth days of pregnancy. At this period other important reactions are taking place in the body.

Thus Browne and Venning (1936), and Evans, Kohls and Wonder (1937) found that the excretion of gonadotropic substances in urine rose sharply between the fortieth and fiftieth day after the last menstrual period. The maximum concentration of this hormone occurred between the fiftieth and sixtieth day and then fell rapidly between the sixtieth and eighty-fifth day and then more slowly to the one hundred and twentieth day being thereafter maintained at this low level. MacGregor and Stewart (1939) however, found that the excretion of gonadotropic substance rose slightly toward term.

Pregnandiol glucuronidate is excreted in the urine of pregnant women. It is regarded as an inactive product of progesterone. MacGregor and Stewart showed that in a normal pregnancy the pregnandiol excretion is relatively high between the sixtieth and eightieth days of pregnancy. Thereafter it falls to a relatively low level, at which level it remains until about the two hundred and fortieth day; then it rises rather sharply and is maintained at this level until immediately before parturition. The results of MacGregor and Stewart differ from those of Browne, Henry, and Venning (1937), in that the former investigators found a high early level, whereas the latter showed a low early excretion. Browne, Henry, and Venning, however, point out that they were unable to establish the limits of normal variability.

Again, Smith and Smith (1938) studied the metabolism of estrogens in woman. They state that from the time of the second missed period the excretion of estriol is increased at a much more rapid rate than that of estrone, resulting in a higher ratio of estriol to estrone. Preceding delivery the estriol excretion dropped off markedly and there was a concurrent augmentation in the potency of the estrone fraction.

Superimposing the curves of MacGregor and Stewart on our own, both the excretion of the gonadotropic hormones and of pregnandiol correspond very closely with the structural alterations taking place in the corpus luteum during pregnancy especially at the "critical" period. This paralleling of the biological and morphological findings occurs with such regularity that it cannot be regarded as being fortuitous.

It seems to us that the first 80 days of pregnancy is a "critical" period and is deserving of more intensive investigation than it has hitherto received. If we could at the same time follow histologically the reactions of the human uterus at this period, as Wislocki and Streeter (1938) have done in the Macaca rhesus, there is little doubt that we would be in a better position to determine the factors responsible for early implantation and the altered metabolism that takes place in early pregnancy.

SUMMARY AND CONCLUSIONS

The gross anatomical and histological features of 13 cases of corpora lutea of intra-uterine pregnancy have been described. Attention is drawn to the importance of examining fresh material, otherwise the very labile cellular inclusions like the lipoid and colloid rapidly disappear after death or after removal from the body.

Corpora lutea removed from patients with ectopic pregnancy, in whom the embryo or fetus is dead, exhibit structural alterations in the contents of the lutein cells and the central cavity.

A curve of the growth of the corpus luteum throughout pregnancy has been constructed. The corpus luteum increases rapidly in size after the fiftieth day of pregnancy. This is maintained until the sixtieth day when it diminishes in size due to the gradual obliteration of the central cavity and a diminution in thickness of the fibrous tissue surrounding the cavity. The lutein tissue remains fairly constant in size throughout the course of pregnancy.

Special attention is drawn to the development of a central cavity containing a potent hormonal fluid.

The theca-lutein cells reach their greatest development at the second to third month and disappear shortly after the obliteration of the central cavity. The granulosa-

lutein cells persist throughout pregnancy.

The two types of cells contain secretory granules, lipoid and chromidial substance but the granulosa-lutein cells contain in addition vacuoles and colloid droplets.

Curves of the incidence of lipoid, secretory granules, and colloid droplets have been constructed. These show that lipoids and secretory granules are most numerous in the early months of pregnancy and diminish toward term, whereas the colloid droplets are few in the early months of pregnancy and increase steadily until term.

Chromidial substance diminishes with the progress of pregnancy.

The secretion of the granulosa-lutein cells appears as non-stainable secretion in vacuoles which are distributed most abundantly in the cells occupying the inner third of the lutein wall close to the fibrous layer separating the lutein cells from the central cavity. Stagnation of the contents of these vacuoles leads to the formation of the stainable colloid. Colloid is not absolutely specific of pregnancy since 0.75 per cent of the cells contained colloid in a corpus luteum which was removed on the day just preceding the next expected menstruation.

Calcium salt may be deposited in the colloid; this is regarded as a further degeneration of the colloid droplets.

The function of the gravid corpus luteum is re-examined. The accepted viewpoint that the gravid corpus luteum begins to involute only in the second half of pregnancy is called into question, and it is suggested that involution may have commenced as early as the second month of pregnancy.

Special attention is drawn to the fiftieth to sixtieth day of pregnancy which we have termed the "critical" period of pregnancy. At this particular time the corpus luteum undergoes marked structural changes which parallel the metabolic disturbances in the body as indicated by the excretion in the urine of pregnandiol, gonadotropic substances, and the three estrogens—estrone, estradiol, and estriol.

The histological criteria diagnostic of the gravid corpus luteum are shown in the accompanying classification.

HISTOLOGICAL CRITERIA DIAGNOSTIC OF GRAVID CORPUS LUTEUM

	Early months	*Later months*
Cavity	Present	Absent
Theca-lutein cells	Present	Absent
Lipoid	Numerous fine droplets; occasional cells with large discrete droplets filling cell which may contain cholesterol.	Diminished; cholesterol containing cells absent.
Secretory granules	Numerous	Diminished
Vacuoles	Very numerous	Greatly diminished or absent
Colloid	Present as small occasional droplets in 6 to 15 per cent of cells Not calcified.	Greatly increased; larger and more numerous in each cell. May become calcified.

We wish to record our indebtedness to Professor R. A. Dart for his constant criticism and advice and for placing the resources of his department at our disposal; and also to Dr. G. Buchanan for his interest and encouragement.

We are deeply appreciative of the material assistance given by Professor James Black, Dr. Krige, Dr. Mes, and especially Dr. G. Spence Smyth who supplied us with most of the corpora lutea used in this investigation.

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CARCINOMA OF THE THYROID GLAND

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THE number of proposed methods for classifying malignant disease of the thyroid gland is evidence enough that there is little unanimity of opinion with regard to grouping variations of malignant change in this organ. The published studies also indicate that there are no uniformly accepted criteria for separating definitely benign from early malignant disease in the thyroid gland. Our study has been undertaken to find a means of clarifying this confusion.

The published methods of classifying carcinoma of the thyroid gland vary from a division into scirrhous and medullary types (1), to an arrangement of six groups with several subdivisions (14). Between these extremes, many different methods have been suggested for tabulating the variations in malignant disease in this organ (5, 6, 8, 10, 11, 12). Some are based primarily upon the pathological characteristics while others correlate both the clinical and pathological findings. It is our opinion that a satisfactory classification for malignant disease of the thyroid gland must be one that takes into account both clinical and pathological observations.

We have studied 63 cases of thyroid gland disease, clearly malignant or suspected histologically to be so, and we have grouped this material according to several of the proposed classifications. From this comparison of methods for classifying thyroid gland cancer, we now feel that the one best suited for general use was suggested by Clute and Warren (3) and it is as follows: Group I, (a) Adenoma with blood vessel invasion, (b) Malignant papillary adenocystoma; Group II, adenocarcinoma—(a)alveolar adenocarcinoma, and (b) papillary adenocarcinoma; Group III, (a) squamous cell or epidermoid carcinoma, (b) small cell carcinoma, (c) giant cell carcinoma, and (d) fibrosarcoma.

We have tested the practical value of this classification by studying routine sections of cases seen during the last 17 years. Of the 63 cases in which examinations were made, 54 were accepted as malignant and 9 were benign as will be made clear later. Many of the cases occurred within the past 5 years but since this is primarily a report dealing with the pathological manifestations of thyroid cancer and their correct interpretation, a study of the tissues from these recent cases has been included. All cases are from the service of Dr. George E. Beilby, to whom the authors are indebted for permission to present the material.

The classification of thyroid gland neoplasms is difficult because of the variations in criteria that are employed to differentiate definitely benign, from early malignant, lesions. Thus, Graham (9) stresses blood vessel invasion, while others emphasize the degree of cell anaplasia (12), or invasion of capsule, the presence of mitoses (2), or clinically by recurrence or metastasis of the tumor (7), as aids in recognizing malignant change. In the more advanced group II and group III lesions the problem of pathological diagnosis is less serious because there is general unanimity of opinion of their malignant nature. We do not wish to emphasize differences of opinion in the subdivisions of these groups and we have, therefore, confined our discussion to the development of criteria for recognition of group I tumors. To make certain that we properly interpreted the histological changes for each group in the classification employed, we consulted Dr. Shields Warren, who graciously examined all of the sections and made several suggestions.

The method adopted for this study was to examine the routine sections and tabulate in

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TABLE I.—CLINICAL COURSE OF PATIENTS IN THIS SERIES

	Operation prior to January 1, 1935						Operation January 1, 1935 to March 1, 1940						Clinical Diagnosis	
	No. Cases	Sex	Alive & well	Dead of carcinoma	Dead other	Recurrence	No. Cases	Sex	Alive & well	Dead of carcinoma	Dead other	Recurrence	Benign	Malignant
Group I Malignant adenoma	5	F	3	1	0	0	8	F	7	0	1	0	12	1
Papillary adenocystoma	4	F	1	2	0	0	5	F	3	0	0	2	5	4
Group II Adenocarcinoma	8	F	5	2	1	0	7	6F 1M	2	4	0	1	9	6
Group III Large cell	8	7F 1M	0	8	0	0	4	F	0	4	0	0	1	11
Small cell	4	2F 2M	1	3	0	0	1	M	1	0	0	0	0	5
Totals	29	26F 3M	10	16	1	0	25	23F 2M	13	8	1	3	27	27
Lost	2													

each case a wide variety of pathological changes. Thus for each tumor such facts as variation in tissue architecture, invasion of veins, capsule, or adjacent tissues, and the character of the stroma were recorded. Also enumerated were variations in the cellular morphology, the presence of mitoses, and the degree of anaplasia. These tabulations were studied to learn whether predominance of one or several features could be relied upon to separate benign from malignant lesions. It was found that tumor tissue invasion of veins, capsule, and adjacent tissues constituted the most reliable indications of the presence of malignant disease in the thyroid gland.

In any examination of thyroid gland tissue the first indication of malignant change is departure from normal tissue architecture. Acini are more numerous and compact in some types or show marked papillary formations in others. The presence of solid sheets or cords of cells is an ominous variation from normal. These findings lead to a study of variations in the individual cells, such as abnormalities in the size, shape, staining reactions, and whether or not mitoses can be observed.

If these atypical variations in the tissue architecture and cellular morphology are found to exist, the presence of invasion is the greatest aid in determining whether or not the tumor is malignant. Such invasion, as encountered in routine sections, need not include veins although careful search will usually demonstrate their involvement in malignant cases. In encapsulated neoplasms, definite evidence of extension of tumor tissue into or through the capsule is as important, in our opinion, as vein invasion. In non-encapsulated growths, invasion of adjacent tissues also carries the implication of malignant change. Care must be exercised to prevent confusing epithelial masses caught in the sclerosis of a benign adenoma with true invasion. The penetration of tumor tissue into at least one of these three structures has been found in each of our malignant cases and a study of additional sections has demonstrated vein invasion in those in which capsular invasion was the first indication of carcinoma.

Endothelium covered masses of tumor cells found within a vessel are regarded as indicative of vascular invasion. It has been possible in some cases to study these masses in serial sections and they have been shown to arise from tumor tissue penetrating the vessel wall. The manner in which the invasion of vessel manifests itself in any given preparation depends upon the plane of the section in relation to the entrance point of tumor into vessel. Thus, in some cases one may see cross-sections of papillary ingrowths which appear to lie free in the lumen of the vessel. To avoid mistaking artefacts for true invasion of veins within the substance of a tumor, it is necessary to demonstrate the site of penetration of the vessel wall; however, a large capsular vein

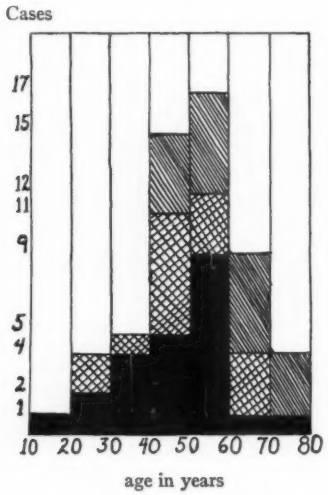


Chart 1. Age distribution for each group. Black area, Group I; cross hatched areas, Group II; diagonal lined areas, Group III.

filled with tumor tissue should be looked upon as evidence of vascular invasion even though the point of entrance of tumor is not seen.

Figures 1 and 2 indicate types of abnormal appearing thyroid epithelium that may be confused with malignant disease. Nine such tumors have been carefully examined and eliminated from this report because close study revealed that the adenomas did not invade their capsules or surrounding tissues and showed no evidence of invading veins. We direct attention to this group because of the diagnostic problem it presents to the pathologist. Some adenomas so closely resemble malignant tumors that even experienced pathologists differ in their opinions. Figures 3 and 4 illustrate such a tumor. In these borderline cases a study of several sections, preferably serial, in addition to the routine preparations, is necessary before the pathologist can differentiate benign from malignant lesions. To enable the pathologist to give an opinion based upon all significant evidence available, a brief clinical abstract should be sent with the specimen. Attention to this detail will give the pathologist a better opportunity to interpret the histological changes and will immeasurably increase the value of his report.

In group I were 22 patients representing 40 per cent of the entire series. It is of interest to note that 2 of the deaths and 3 of the 4 recurrences took place in patients presenting the papillary adenocystoma type of tumor. Two recurrences, one listed as dead of carcinoma in Table I, occurred 5 years after operation. Two other recurrences, one listed as dead of carcinoma in Table I, occurred 3 years after operation. The 4 patients living beyond the 5 year period have survived 9 to 11 years. The patient alive 9 years after our operation had an adenoma of the thyroid gland removed in December 1920. Through the courtesy of Dr. J. L. Donhauser and Dr. J. J. Clemmer, of Albany, the slide from the original tumor has been made available for our study. We regard the lesion as a malignant adenoma with vein invasion. This patient, therefore; has had a recurrence after 10 years, and by its removal an arrest of the disease for 19 years.

In group I were 13 adenomas with evidence of vein invasion. These arose in so called fetal adenomas and exhibited closely packed acini. Nine tumors were of the papillary adenocystoma type. These were characterized by one or two layers of epithelial cells covering finger-like projections of stroma. This histological feature was not always associated with gross cyst formation. The invasive qualities of these two types of tumors, as indicated by their extension into veins, capsule, or adjacent tissues, must be demonstrated before they may be included in this group as truly malignant tumors.

There were fifteen patients in Group II, 27 per cent of the series. There were 6 patients who lived 5 or more years although 1 died 6 years after operation from Parkinson's disease and arteriosclerosis (listed as dead of other disease in Table I). Of the 5 remaining, 2 have lived 8, 1 has lived 10 and 2 have lived 11 years. These 6 cases represented 75 per cent 5 year cures, but the fallacy of small numbers was obvious. Four of the 6 deaths in this group occurred in patients operated upon less than 5 years ago. One of these died after operation.

The adenocarcinomas in group II were either alveolar or papillary in type and exhibited more easily recognized malignant dis-

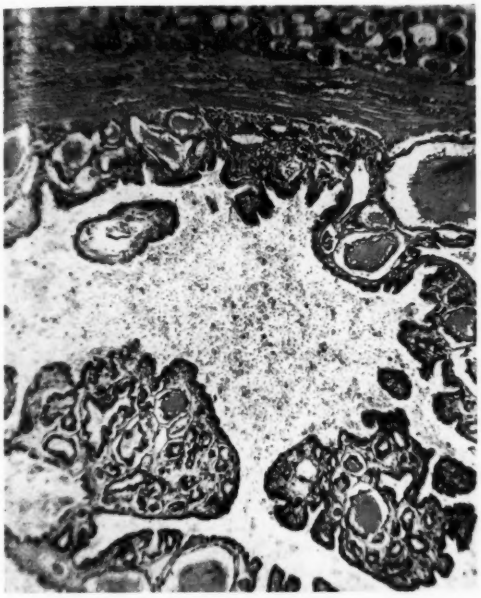


Fig. 1. Benign papillary adenocystoma.

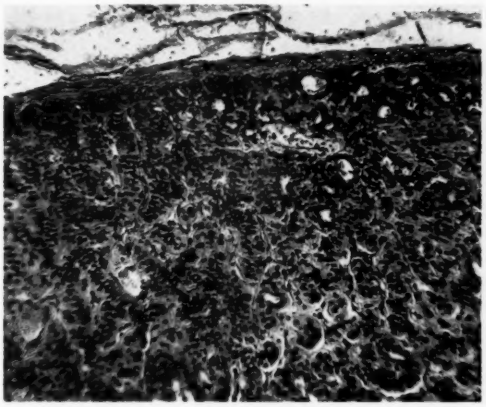
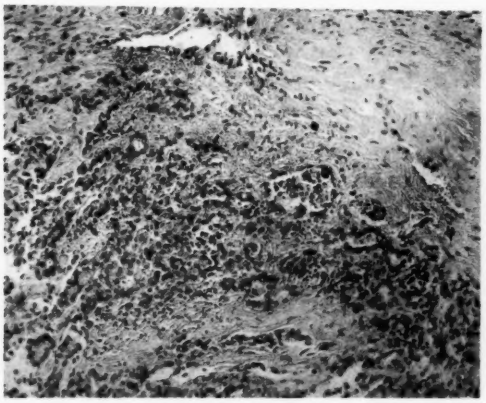


Fig. 2. Benign adenoma.

ease. It is at times hard to differentiate between the more malignant cases in group I and true adenocarcinomas. A distinguishing feature according to Warren is the presence of broad sheets of anaplastic cells.

In this series, group III was represented by 12 cases of large cell carcinoma and 5 cases of small cell type, which together were 31 per cent of our cancer patients. We have not seen the squamous cell type. One patient has lived for 6 years following her operation and a second patient has survived 3 months. Both of these patients had the small cell type of carcinoma and in each the operation consisted of biopsy followed with deep x-ray therapy. All



Figs. 3 and 4. Borderline malignant adenoma. Some experienced pathologists regard this tumor as benign; others consider it malignant.

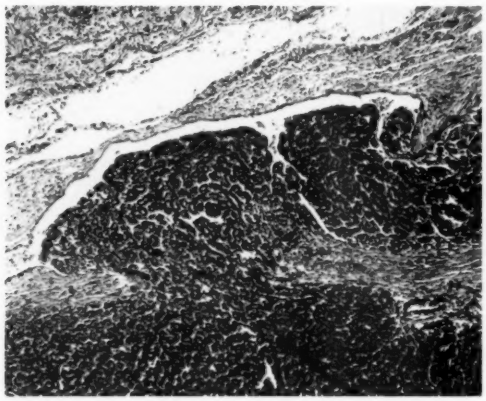


Fig. 5. Recurrent malignant adenoma showing blood vessel and capsule invasion.

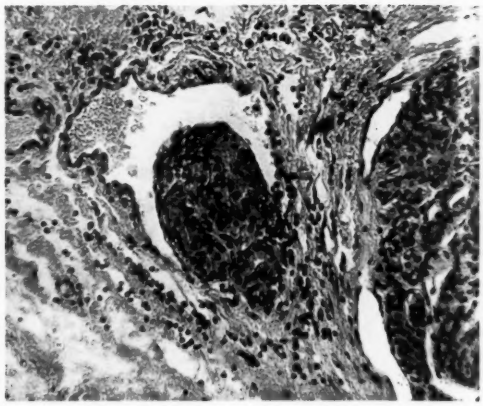


Fig. 6. Recurrent malignant adenoma growing into a blood vessel.

other patients in this group are dead now but lived for an average of 8.3 months after operation, with a maximum of 17 months. One died after operation.

The histological changes of tumors in group III leave no doubt as to the malignant nature of the process, but in certain lesions there is difference of opinion as to whether the tumor is of ectodermal or mesodermal origin. Further investigation is necessary to answer this question.

In this series of cases treatment consisted of excision whenever possible. In clinically inoperable cases a biopsy was taken and deep x-ray therapy advised. The fact that this entire series has been treated by one individual adds value to the results obtained.

In group I, x-ray treatment has been employed in recent cases only; 1 for a recurrence with ultimate death, 2 following excision of a recurrence, and in only 1 case following the primary operation. All others in this Group were subjected to subtotal thyroidectomy with removal of the tumor.

In group II, 3 cases, clinically inoperable, were treated by deep x-ray therapy after biopsy. Two are dead and one still lives with known metastases to bone. A recent case has been treated after the primary removal of the tumor.

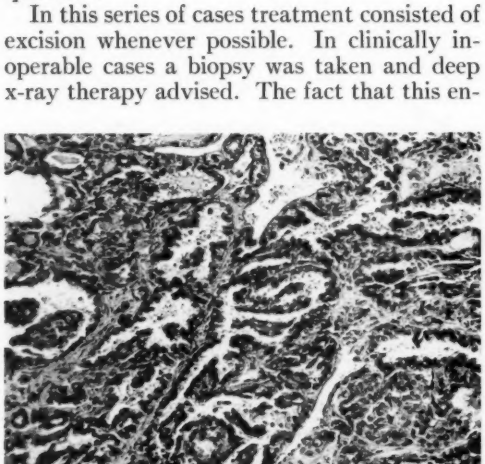


Fig. 7. Papillary adenocarcinoma.

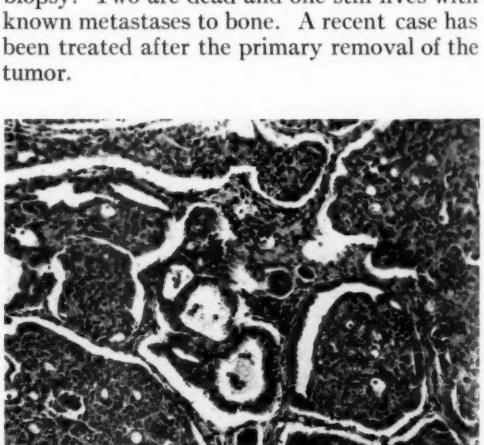


Fig. 8. Alveolar adenocarcinoma.

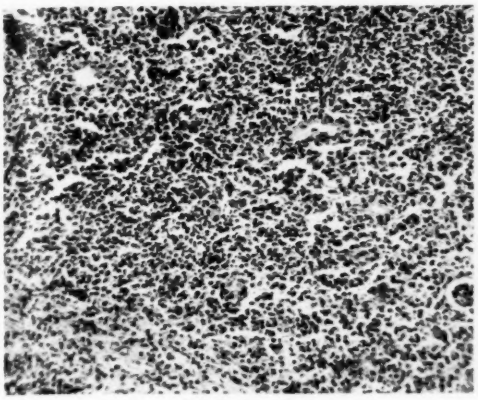


Fig. 9. Small cell carcinoma.

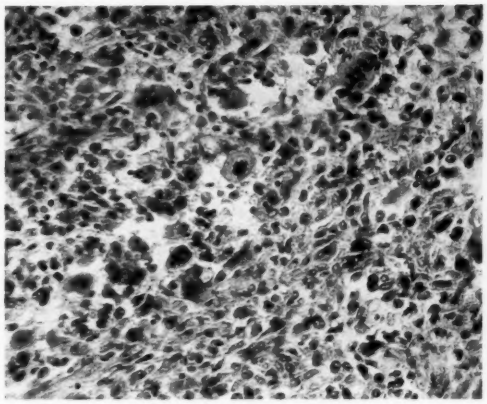


Fig. 10. Giant cell carcinoma.

Group III cases were nearly all treated prior to the modern, multiple small dose method of roentgen therapy. One patient is alive more than 6 years and received 1,100 r in 6 treatments. All others are dead except one patient operated upon during January, 1940.

We agree with many that surgical removal of the cancerous gland in combination with some form of irradiation offers the patient the greatest hope for permanent arrest of this disease. When the pathological examination reveals malignant change in an adenoma clinically considered benign, the prognosis must be guarded. Because of this uncertain outcome, we can not agree with those (13) who feel that deep x-ray therapy is unnecessary for this type of case.

General considerations of this series as a whole revealed no new features. The age distribution (Chart 1) was in keeping with the published statistics. The sex was of interest only so far as 4 of the 5 males in this series were found to have the most malignant form of thyroid carcinoma. The incidence of cancer in relation to all thyroid operations for the period covered by this study has been 1.5 per cent. In relation to nodular goiters only, the incidence of cancer was 3 per cent. Forty-one of the 54 patients gave a history of goiter for one or more years prior to the time of the operation.

The lack of a standard terminology in the classification of thyroid gland cancer, makes statistical comparisons with the reports of other authors a dangerous practice, because of the uncertainty of properly interpreting the criteria employed. We have already indicated how we made certain that we understood the criteria for the classification we have used and we can safely say that our study has confirmed the practical value of the classification of Clute and Warren.

We emphasize that this method of grouping thyroid cancer cases conveys definite prognostic information to the clinician. Thus cases in group I, show pathological characteristics that result in low mortality, while the highest death rate is to be expected in cases with the features of group III. We have indicated the

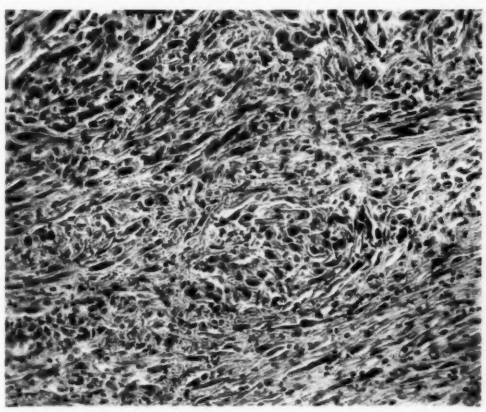


Fig. 11. Giant cell carcinoma, spindle form sometimes confused with sarcoma.

discrepancies of our small series in comparison with reports of larger numbers of cases (6), in which for example, the prognosis in group I is for a 5 year survival in about 80 per cent of the patients. Even with this rather good outlook deaths from these tumors do occur and recurrence of the disease after long intervals may take place. Group II neoplasms are ultimately responsible for death in approximately 66 per cent, when a sufficient number of cases are analyzed. The correct diagnosis of a group III tumor carries with it the prognosis of death within a year to all such unfortunate patients with but rare exceptions.

In this presentation attention has been called to the multiplicity of the classifications of thyroid gland carcinoma, and the belief is expressed that a lack of uniformly accepted criteria for the pathological diagnosis of malignant disease in this organ may be, at least in part, responsible for the confusion. It may be due in part to the fact that very few investigators have had an opportunity to study a series sufficiently large to be of statistical value. It is apparent, however, that very little advance toward a solution of the problem of pathological diagnosis of thyroid gland carcinoma has been made since the report of Graham in 1924 when he stressed the importance of blood vessel invasion but also indicated the importance of capsule invasion as a criteria for malignant change. We have not been able to discover any new criteria from the study of this small series, but we have indicated the practical value of relying upon evidence of tumor tissue invasion of surrounding structures as encountered in routine sections.

The authors admit the inadequacy of numbers in this study and do not therefore, draw specific conclusions. In our opinion it is desirable to plan a method of concerted study that will lead to conclusions which will warrant uniform acceptance. Such a plan would be based upon a collection of all material possible gathered together in one place with statistical interpretation by experienced pathologists.[1]

[1]This plan was presented in detail to the Executive Council of the American Association for the Study of Goiter at its meeting April 15-17, 1940. The Council of the Association appointed a committee to study the problem.

SUMMARY

1. The classification of thyroid gland cancer is not entirely satisfactory, possibly because of the lack of uniformly accepted criteria.

2. Fifty-four cases of thyroid gland carcinoma have been analyzed to determine what future studies may help to clarify this confusion.

3. From this analysis it appeared that a statistical study of a large number of tumors collected from all possible sources must be made to assure uniform acceptance of the criteria for, and the classification of, malignant disease of the thyroid gland.

The authors acknowledge their indebtedness to Dr. Arthur W. Wright for many helpful suggestions during this study.

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THE TRANSPLANTATION OF SKIN AND SUBCUTANEOUS TISSUE TO THE HAND

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THERE are many clear cut indications for transplanting normal covering tissue from one part of the body to another, and in particular from a distant part of the body to the hand. Flame and hot water burns, electrical burns, destruction of covering tissues as a result of severe infection or excessive irradiation, crushing and avulsing injuries, burns due to powerful chemicals all occur with distressing frequency in the practice of every surgeon. To replace the destroyed tissue with normal tissue *at the earliest moment that it can be safely accomplished* is a sound surgical principle. Time, expense for hospital and patient, and, most important, function will be saved if raw surfaces are covered as early as possible with some form of graft or flap.

One cannot forget, however, that, if a patient's vitality is below normal, transplanted tissue heals with difficulty. Long continued suppuration, repeated losses of small amounts of blood, perhaps lack of good food, are all important factors. If a patient's reparative processes are at a standstill a graft, in particular, taken from one part of the body and temporarily deprived of its blood supply cannot be expected to heal over a raw surface. Blood transfusion, sunshine, ultra-violet radiation, vitamin therapy, and good food are all of value in making the patient a better operative risk.

In determining what procedure should be followed in a specific case several general principles should be kept in mind:

1. The fate of the transplant depends upon the development of an adequate blood supply before cellular starvation and resulting necrosis take place. The thinner the graft the more certain it is to survive, simply because there are fewer mouths to feed. The more tissue one attempts to transplant the greater is the need for nutritive blood serum to maintain life. With each added micron of thickness there is an added hazard that a graft (and by a graft, as distinguished from a flap, is meant tissue which is completely detached from its original blood supply and transferred to a new site) will not survive.

2. In direct contrast with the advantages of the thin graft from the standpoint of certainty of "take" are its disadvantages from the standpoint of functional result. The thinner the graft the less adequately it protects the underlying tissue; the more easily it breaks down when subjected to irritation or trauma; the more certain it is to contract and when laid over a flexor surface to favor development of a flexion contracture. With each added micron of thickness there is added assurance that the graft, if it survives, will give a satisfactory result from the standpoint of function, appearance, and freedom from tendency to contract.

3. Weighing the advantages and disadvantages of grafts of varying thickness it is obvious that the thicker the graft that can be applied with assurance of survival the more satisfactory will be the final result. If the raw surface is successfully covered, however, a graft which is too thin to form an adequate protection can be excised at a later date and a full thickness graft or a pedicled flap substituted for it with every assurance of success, because the newly formed raw surface will be free from infection. If one attempts to transplant too thick a graft and it fails to survive, nothing is gained, valuable time is lost, and the raw surface still remains as an open wound, a potential atrium for further infection, and a site for the formation of the inevitable scar tissue which constantly forms as healing progresses.

4. Certain structures require for their protection and normal function a covering of subcutaneous tissue as well as skin, and we

From the Division of Surgery, Northwestern University Medical School. Read before the Minneapolis Surgical Society, Minneapolis, Minnesota, February 1, 1940.

know of no way of transferring subcutaneous tissue with its covering skin except by the use of a pedunculated flap. Furthermore, these same structures—tendons, nerves, the walls of blood vessels, bones, joint capsules—are so poorly supplied with blood vessels that a graft, as distinguished from a flap, laid over them cannot be expected to survive, simply because there is so little vascular tissue from which new capillaries can develop to provide a blood supply for the newly transplanted tissue.

5. Any one of several complicating factors may add a sufficient handicap to make survival of the transplant impossible. Chief of these is infection, and so disastrous is the effect even of a low grade infection that we never attempt to lay a whole thickness graft over a granulating surface or the yellow base left by the excision of exuberant granulation tissue, no matter how healthy the granulations appear or how excellent the condition of the patient. Furthermore, only in unusual instances are we willing to lay a flap, with an assured blood supply through its pedicle, over a granulating surface, so concerned are we over the destructive effect of even a few bacteria on the vulnerable subcutaneous tissue which forms the undersurface of the flap.

6. The extravasation of only a small amount of serum or blood underneath a graft may form an impassable barrier to the ingrowth of budding capillaries. If every square millimeter of the graft is pressed smoothly against the underlying raw surface and held in position with accurately placed sutures and a pressure dressing, such extravasation is unlikely to occur and the most favorable conditions for rapid formation of the new capillary network are afforded. No one has emphasized these facts more persistently and effectively than Blair, Brown, and their associates and no one has described so well the various methods available for maintaining pressure over a graft or demonstrated so conclusively its importance in securing good results.

7. It is to Blair and Brown, too, that we are indebted for constant emphasis on the importance of clean cut excision of redundant granulations so as to provide a smooth yellow base over which to apply a graft of intermediate thickness. If an infected wound has been dressed with scrupulous cleanly care from day to day and with the constant application of sponge pressure outside the sterile dressing, the granulations may become so firm and healthy that no excision of granulation tissue is necessary. Frequently, however, some exuberant growth and congestion develop, and a soft, congested, granulating surface, which projects above the level of the surrounding skin, does not form a favorable base upon which to lay a graft.

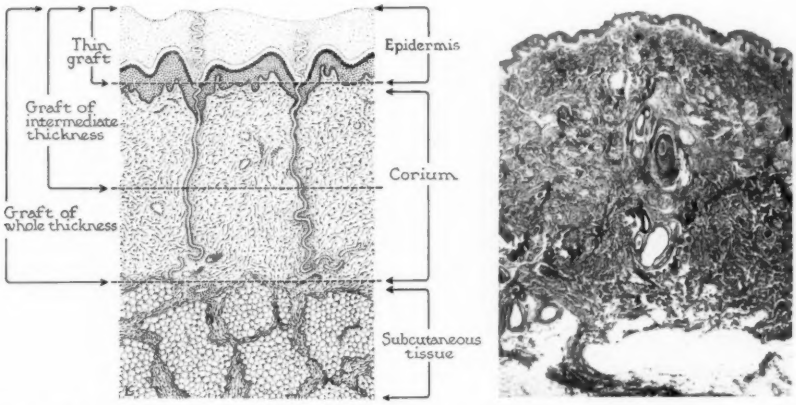

Fig. 1. Diagram showing skin in cross section, and thickness of skin included in different types of graft. In the photomicrograph of a similar section of skin, at the right, can be seen the numerous epithelial elements within the corium—hair follicle, sebaceous and sweat glands, from which the epidermis is rapidly reformed, even though the entire epidermis and a part of the corium have been removed for use as a graft.

For the great majority of cases with a surface defect of the hand we have come to depend upon one of three types of transplant: the graft of intermediate thickness, the graft of whole thickness skin, and the pedunculated flap (Fig. 1). Rarely the thin graft with little derma and the pinch grafts of Reverdin or the thicker grafts of Davis offer advantages over the graft of intermediate thickness.

THE GRAFT OF INTERMEDIATE THICKNESS

The indications for the use of this type of graft and the technique of its application have been presented in such comprehensive fashion by Blair and Brown in a classical paper in SURGERY, GYNECOLOGY AND OBSTETRICS[1] and in a more recent paper by Brown in the *Annals of Surgery*[2] that it would be both presumptuous and wasteful of printer's ink to discuss the subject at length. In covering raw surfaces on the hand the graft of intermediate thickness has a wide field of usefulness. It can be laid over a clean granulating surface or over the yellow base left by the excision of redundant granulation tissue. In other words, it can be used advantageously for the patient who has suffered an extensive burn, a crushing or avulsion injury, or an infection with loss of tissue as soon as the raw surface is clean and the patient's general condition permits (Figs. 2, 3). It can be used to cover freshly made raw surfaces, *if the patient is seen within a few hours* of the time of injury, and if there is still subcutaneous tissue present in the floor of the wound to provide a source of blood supply and to protect the important deeper structures—tendons, nerves, and blood vessels. An often neglected opportunity for the application of such a graft, as emphasized by Reed and Harcourt, is after traumatic amputation of a finger tip (Fig. 4) crushed between a door and its frame or caught in a punch press.

Because such a graft can survive, even if there has been some impairment of blood supply of the surface over which it is laid, it is often possible to apply a graft of intermediate thickness immediately after excision of skin damaged by excessive irradiation, if sufficient time has been spent before operation to control the infection which is invariably present on the surface and in the deeper layers of the skin (Fig. 5). Even if a part of the graft fails to survive, complete healing can usually be secured by careful and cleanly after-care and, if necessary, a second graft can be laid over small raw surfaces that fail to show rapid tendency to heal from ingrowth of adjacent epithelium.

[1] 1929, 49: 82–97.
[2] 1938, 107: 952–971.

Fig. 2. Flame burns of both hands first seen 3 weeks after injury. Grafts of intermediate thickness were applied after 9 days of treatment to overcome infection.

Fig. 3. Result of application of grafts of intermediate thickness for flame burn of forearm.

In preparing a raw surface for application of the graft we have come to rely on cleanly surgical care of the open wound, the constant application of moderate pressure over the raw surface, and rest with the aid of light aluminum splints. In dressing the wound every effort is made to avoid constant tearing down of healing tissue by rough treatment and abrupt tearing away of dressings. The raw surface is cleansed by irrigation with salt solution and gentle sponging. Tissue which is obviously necrotic is cut away without cutting into healthy granulations. The area about the wound is kept clean and free from crusts and epithelial débris by soap and water cleansing. In dressing the wound at least one layer of very fine meshed gauze, such as old handkerchief linen or very fine meshed muslin, is laid directly over the raw surface. Fine meshed gauze does not readily permit growth of granulation tissue into its interstices. If the newly formed tissue does not adhere to the overlying dressings it is not repeatedly traumatized and broken down as the dressings are changed.

The fine meshed gauze over the wound and a few additional layers of flat gauze are moistened with sterile boric or salt solution so as to provide a moist dressing and favor drainage of wound secretion into the dressings. Oily dressings and dry dressings favor retention of wound secretion and the formation of small accumulations of pus which act as culture tubes for the rapid growth of any bacteria present.

Over the moist dressings are laid dry sterile dressings in sufficient thickness to permit absorption of all wound secretion. Over the dry dressings are bandaged clean soft marine

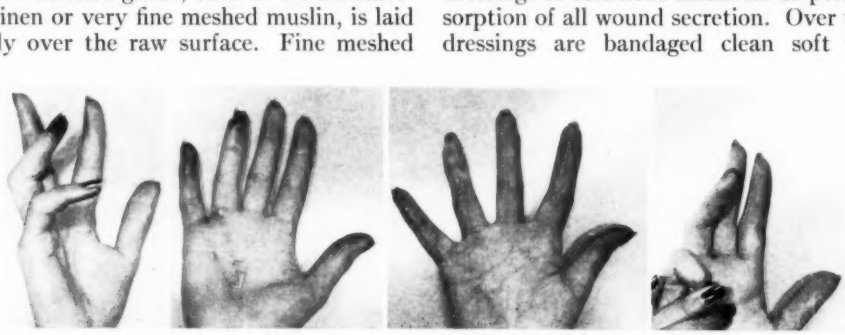

Fig. 4. Result of application of graft of intermediate thickness 48 hours after partial amputation of tip of ring finger. (Patient was first seen 2 days after injury.)

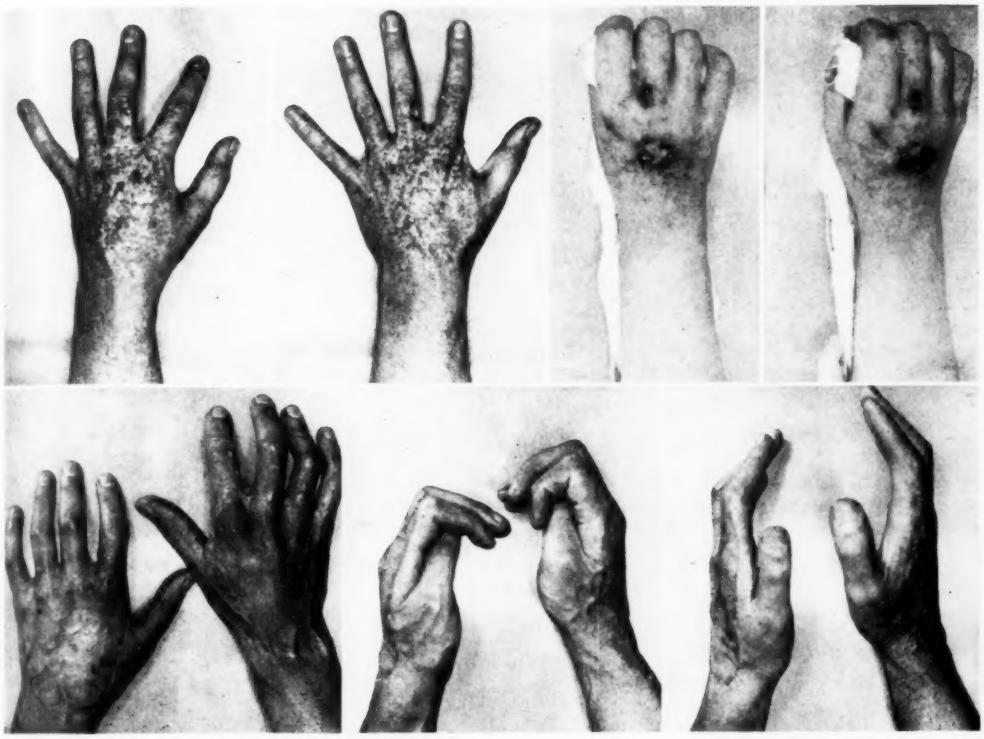

Fig. 5. Result of application of grafts of intermediate thickness for irradiation dermatitis and ulceration developing over a period of 9 years. Result 8 months after operation on right hand, 4 months after operation on left.

sponges in sufficient number and with sufficient pressure to provide a moderate pressure over the entire wound surface. The bandaged hand is immobilized in a light splint, and in such a position as to favor function. If the raw surface involves the dorsum of the hand the fingers are bandaged in semiflexion; if the palm is affected, in extension.

It may surprise the skeptical individual to learn how quickly a "dirty" hand with an extensive wound partially covered with sloughing skin, with dried crusts and with fragments of tissue coagulated by tannic acid can be converted into one suitable for the application of a graft by simple cleanly treatment, the application of pressure over the dressing and continuous rest obtained with the aid of a splint.

At the time of operation the donor site is prepared with plain white soap and water and without antiseptics. We believe it is good technique to secure the graft as soon as the donor site is prepared and the field draped, to fold it in moist gauze so that only the epithelial surface is exposed, to apply a smooth snug pressure dressing over the donor site with a few thicknesses of fine meshed gauze saturated with petrolatum next to the raw surface, and, while the surgeon stands aside, to have one member of the team remove the dressing from the hand and irrigate the area to be covered with warm salt solution. If the dressings have been carefully done in the days before the operation little cleansing of the hand should be necessary in the operating room. The more rapidly the graft can be applied to the raw surface after the pressure dressing is removed, the less opportunity is there for congestion of granulation tissue to develop. We have sometimes seen large raw

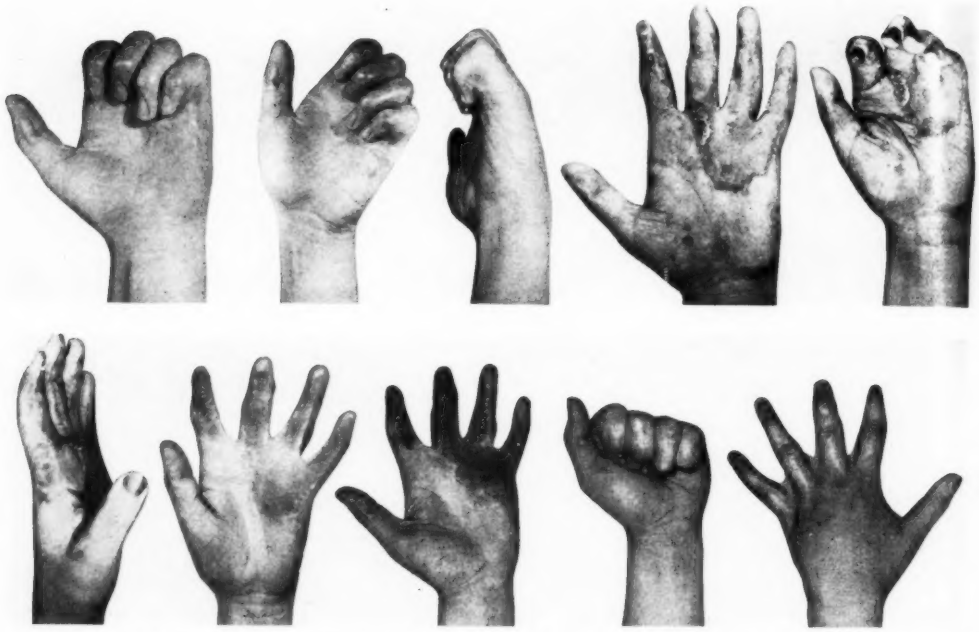

Fig. 6. Mangle burn resulting in destruction of palmar skin to very tips of fingers. Immediate result and result 11 months after application of grafts of whole thickness skin, and of a small flap to distal phalanx of index finger.

surfaces which appeared red and firm immediately after the pressure dressing was removed become dusky and congested while the surgeon was cutting grafts with which to cover them. If firm red granulations cover the open wound and the raw surface forms a slight concavity instead of projecting above the level of the adjacent skin edges, the graft is laid directly over it without further preparation. If excessive granulation tissue is present, it is shaved away as smoothly as possible.

It is advantageous to cover the raw surface with a single graft which projects a little beyond the margins of the raw surface. Time is lost and the operation becomes much more difficult if several grafts must be applied and anchored in place. To secure a graft of adequate size the suction boxes and long thin knives devised by Blair are very helpful. The device of Padgett and Hood for holding the skin taut and securing a graft of uniform thickness makes a simple procedure of what otherwise calls for skill and long experience.

The importance of anchoring the graft securely and under tension, of providing a few openings for escape of serum from underneath it, and of applying the dressing in such a way that every square millimeter is firmly apposed to the underlying surface has been frequently stressed by Blair and Brown, and these details are of importance in assuring success.

At times, particularly if we are uncertain as to whether infection is completely under control, tubes of the Carrel type are incorporated in the dressing so that it can be kept moist by 4 or 6 hourly injections with salt solution without disturbing the dressing or releasing the pressure. The open ends of the tubes are protected with sterile gauze, and the nurses in charge are carefully instructed concerning the importance of not adding contaminating organisms by careless technique in the injection of the solution.

If the graft has been laid over a granulating surface or over the raw surface left by excision of irradiated skin the primary dressing

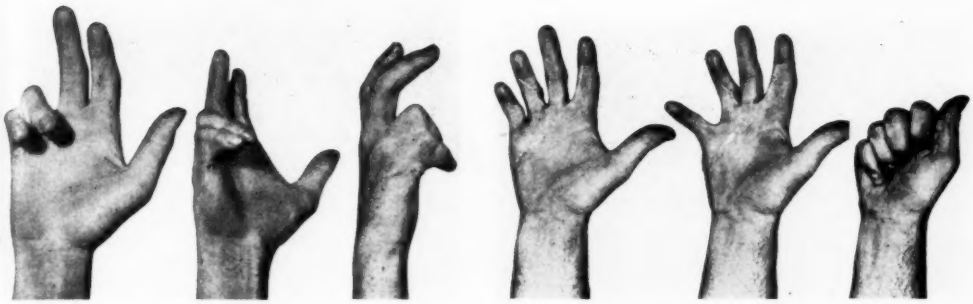

Fig. 7. Contracture following a burn sustained at age of 3 years, operated upon unsuccessfully 4 years and 8 years afterward. Appearance of hand at age of 23 years and result after application of graft of whole thickness.

is left undisturbed for 4 or 5 days; and for as long as 8 days if the graft has been laid over a recent wound and if no symptoms of developing infection—fever, redness and swelling above the involved area, throbbing and pain—have appeared.

The first dressing is removed with every care to avoid tearing away healing epithelium. Sutures are removed, and any redundant portions of the graft are cut away. If the graft is pink and dry a simple dry dressing or a petrolatum gauze dressing is reapplied and pressure is maintained over the wound for another 4 or 5 days. If any small pools of pus or wound secretion are present they are wiped away with sterile applicators and the same type of moist dressing is applied that was used during the pre-operative period. The dressing is then changed once daily, and the pressure and splinting are maintained until healing is complete and every square millimeter of raw surface covered with epithelium.

If loss of a portion of the graft 1.5 centimeters, or more, in diameter takes place a second graft is applied as soon as necrotic tissue has separated and the raw surface is again red and healthy. Though this may not often be necessary it is just as logical not to wait for spontaneous healing of such a raw surface as it was in the case of the original wound.

A word should be added concerning the pinch graft or small deep graft. To us it has seemed that there are few indications for their use. It has been our misfortune to have seen rather frequently the site of an extensive burn or avulsion injury covered with uneven, pock-marked epithelium; and to have been often confronted with patients with large raw surfaces still uncovered in whom practically every available donor site has been converted into irregular areas unsuitable for use as the source of a graft of intermediate thickness. Today the use of the Reverdin graft frequently seems a makeshift substitute for a good

Fig. 8. Result of application of graft of whole thickness skin for burn contracture of palm, and of similar grafts to overcome residual syndactylism.

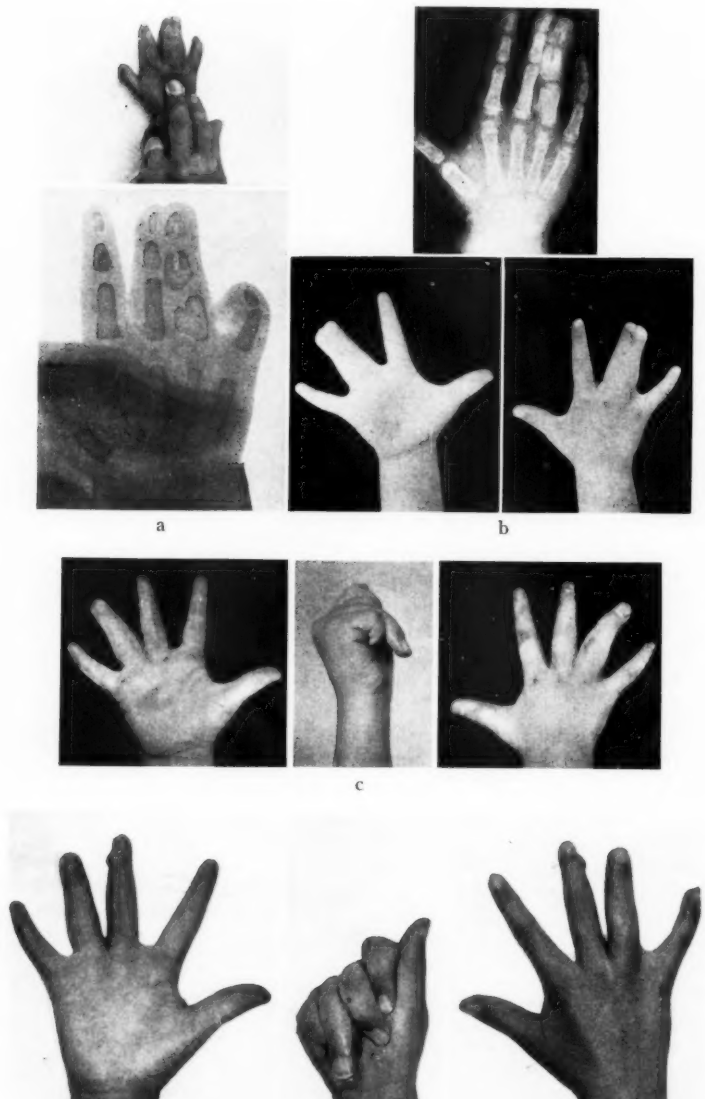

Fig. 9. Syndactylism of middle and ring fingers. a, Appearance at age of 1 year; b, at age of 4 years. c, Result immediately after operation and d, 2 years later.

surgical job. We would use it only in patients unable to take an anesthetic and in whom there might be some advantage in planting a few islands of epithelium in the middle of a raw surface; and in patients with an anaerobic streptococcic infection, such as Meleney has described, in whom there would be a definite risk in covering the entire raw surface at one time and applying over it an occlusive dressing.

THE GRAFT OF WHOLE THICKNESS SKIN

The indications for the use of this graft and the technique of its application have been very fully and clearly presented by a number of American surgeons—notably by Blair and J. S. Davis; more recently by Garlock, Dragstedt and Wilson, MacCollum, Conway and by Dufourmentel and Tierny of France.

In surgical conditions involving the hand we have found the graft of whole thickness skin of particular value in the treatment of contractures resulting from burns, in the treatment of syndactylism, of Dupuytren's contraction, of irradiation dermatitis without ulceration, and occasionally in the immediate repair of wounds following crushing or avulsion injuries.

Burn contractures. Rarely does one encounter such thick keloid-like scar tissue as forms over the palmar surface of hand and fingers following a deep burn; and particularly so if during the process of healing efforts have been made to keep the fingers extended by some form of tension splint. Fortunately for patient and surgeon the tough and resistant palmar and digital fascia acts as a barrier to protect the deeper lying tendons and nerves, so that in most instances of burns of the palmar surface one can still find after complete excision of the dense covering scar a thin layer of fairly normal connective tissue covering tendon sheaths, nerves, and blood vessels. In such a case the graft of whole thickness forms the simplest and most satisfactory method of covering the raw surface (Fig. 6). Its advantages are many: the operation, though tedious, can be completed in one stage; the graft is accurately sutured to the free margin of the defect so that the wound is closed and postoperative care is reduced to a minimum;

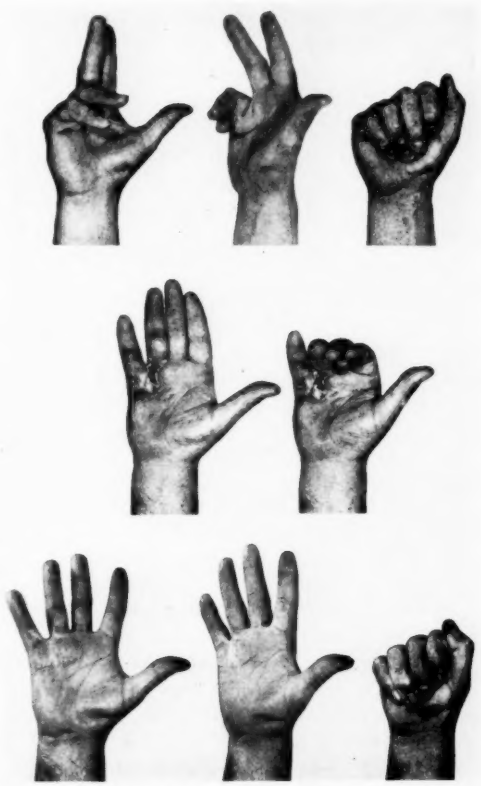

Fig. 10. Result obtained in case of long standing Dupuytren's contraction after excision of contracted palmar fascia and application of graft of whole thickness to replace defect over ulnar side of palm and between little and ring fingers.

the graft can be made to conform to a raw surface of irregular outline and curving base —an important advantage which this graft possesses, as compared with the pedunculated flap, when the web between the fingers is involved and the deforming scar has bound the fingers in an acquired syndactylism (Fig. 7).

As complete excision of contracting scar tissue as it is possible to accomplish is essential for success. This often means a long and tedious dissection and always constant care to avoid tangential injury of digital nerves and blood vessels, often drawn out of their normal position by contracting fibrous tissue. If during the progress of the dissection one constantly holds taut the dense scar tissue as

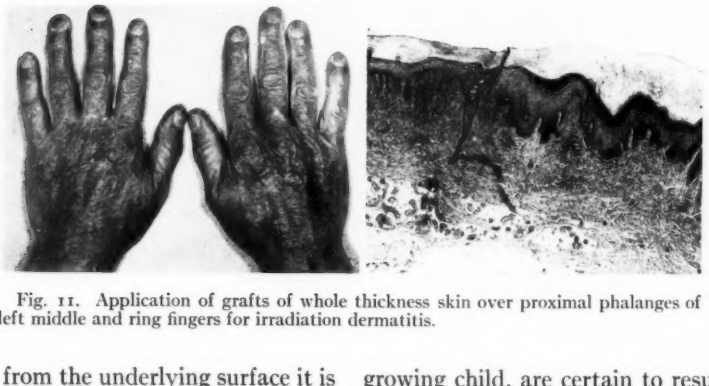

Fig. 11. Application of grafts of whole thickness skin over proximal phalanges of left middle and ring fingers for irradiation dermatitis.

it is cut away from the underlying surface it is easy to cut away a section of a digital nerve under the impression that one is excising only the greatly thickened covering tissue. A bloodless field, secured with the aid of a blood pressure cuff inflated to 260 millimeters, patience, and repeated relaxation of the tension with which the excised tissue is drawn away from the raw surface as it widens during the progress of the dissection help the surgeon to avoid such injury.

In severe flexion contraction of the fingers our greatest difficulty has usually been to excise completely the scar tissue at the sides of the fingers, where the volar digital fascia becomes continuous with the fibrous expansion of the extensor tendon. Here, too, the digital nerves and blood vessels are usually intimately fused with the contracting scar, and the danger of injuring them is especially great. As the dissection is continued and fingers long contracted are gradually drawn into extension the contracted digital nerves and blood vessels may begin to stand out as taut bowstrings. In cases of long standing contracture it requires great care to avoid rupture of these taut slender structures and to provide for them some protective covering of soft tissue.

One can hardly overemphasize the importance of excising the contracting scar so completely that the remaining normal tissues are permitted to retract to their normal position, and so that normal tissue to which the graft can be sutured is present at the margin of the defect. If scar tissue is left behind, some contraction of the suture line and partial recurrence of the contracture, particularly in a growing child, are certain to result. Scar tissue at the margin of the defect also interferes with vascularization of the graft, and the development of a blood supply from the skin margin is an important factor in the healing process.

An exception to this rule of complete excision of scar tissue is made in cases in which such extensive keloidal thickening has developed as a result of constant and repeated tension that complete excision would be inadvisable because of the extent of involvement or because of the patient's physical condition or youth. With thick keloidal masses on the dorsum of the hand, for example, which prevent separation of the fingers from one another but which do not extend to the palmar surface we have seen excellent results, and remarkable flattening of the thick scar tissue left behind, after simple longitudinal di-

Fig. 12.

vision of the keloidal tissue at the clefts between adjacent fingers so as to permit separation of the fingers without tension, and the application of whole thickness grafts over the normal subcutaneous tissue exposed in the "valleys" between the "walls" of scar tissue. Similarly, good results have been secured simply by dividing thick contracting cords over the dorsum of the wrist or over the flexor surface of the elbow and covering with a whole thickness graft the considerable raw surface exposed by the wide retraction of the tissues released from tension.

Syndactylism. The plastic procedures suggested by Zeller, Dieffenbach, Felizet, Didot, Faniel, Rudulesco and others for the care of syndactylism are to us of historical interest only. They appear simple and adequate as described in textbooks of surgery, but we have never seen a successful result from the attempt to make the tissue present on the hand suffice for covering the raw surfaces resulting from surgical separation of completely fused fingers. On the contrary we have seen deformities and contractures with both flexion and lateral deviation, deformities exceedingly difficult to correct, result from the attempt to treat syndactylism by one of these various procedures.

The explanation is simple. When the fingers are separated sufficiently to permit normal abduction there is simply not sufficient tissue available to cover the raw surface. The greatest deficiency, moreover, is at the base of the cleft between the adjacent fingers—the site at which scar formation is certain to produce recurrence of syndactylism. Unless one faces the simple fact that no good result can be obtained by attempting to stretch an insufficient supply of covering tissue over an extensive raw surface, failure is certain to result. Moreover, the necrosis that results from excessive tension along the suture line and the inevitable infection that follows separation of skin edges as sutures cut through them, produce scars that gradually draw the affected fingers into an awkward position and that are exceedingly difficult to remove and counteract at any secondary operation.

Any operation for syndactylism should be postponed until the period of rapid growth is past, unless fingers are being drawn into a lateral deformity by the fusion with adjacent fingers. No matter how deeply the cut is made to separate the fused fingers and how carefully the graft is applied, if the patient is operated upon during the first few years of life, recurrence of the deformity is almost certain to take place because the transplanted tissue does not keep pace in growth with the rapidly growing hand. We would prefer never to operate upon a patient before the age of 4 or 5 years (Fig. 9); and would wait until the age of 10 or 11 if there were no indication of in-

Fig. 12. Result of immediate application of grafts of whole thickness skin to fill defects resulting from crushing injury. (Appearance of hand after injury is shown on opposite page.)

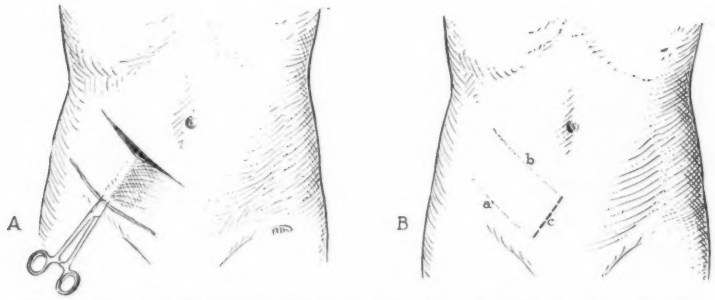

Fig. 13. Diagram illustrating method of raising delayed flap. Flap is cut across at lower end, *c*, after incisions *a* and *b* are healed.

creasing deformity. When recurrence and contracture have developed following an operation performed in infancy, secondary operation is made difficult by the presence of scar tissue and sometimes precarious because of injury of tiny digital blood vessels at the primary operation.

When operation is carried out the separation of the fingers should be carried as deeply as possible without injuring the digital vessels and digital nerves as they separate in Y shaped fashion to pass to the sides of the adjacent fingers. The separation should be carried farther proximalward on the dorsal than on the palmar surface, for as Kanavel emphasized in his scholarly monograph on "Congenital Malformations of the Hand," the floor of the web slopes proximalward from palm to dorsum and this obliquity should be kept in mind in separating the fingers and in cutting the graft.

In cases in which the skin is lax or somewhat redundant at the level of the web, and in which some subcutaneous separation of the fused fingers is possible, we frequently use the relaxed skin and most of its subcutaneous tissue as a pedunculated flap, with its base on the dorsum of the hand, to cover the base of the cleft between the fingers after they have been separated. Two single grafts of whole thickness skin are then applied to cover the remaining raw surfaces on the opposing sides of the separated fingers. The more complete and close the fusion between adjacent fingers the more inclined we are to use the single graft, as described, to cover the entire raw surface.

Dupuytren's contraction. Failure to secure a good result in patients with Dupuytren's contraction is just as certain to result from the attempt to stretch contracted skin over an extensive raw surface as from failure to carry out complete removal of the thickened and contracted palmar and digital fascia. Even in cases in which the skin is not contracted it may be so intimately fused with the thickened fascia underneath it that its vitality is impaired, and if undermined skin is left behind in the hope of avoiding the use of a graft dry necrosis and separation eventually take place with long delay in healing, scar formation, and tendency to recurrence of the deformity.

The use of a whole thickness graft is the simplest and most satisfactory method we have found of replacing hopelessly involved skin, and of making it possible to close the wound without excessive tension when the fingers are again permitted to come into extension as a result of the removal of the thickened and contracted fascia. We have not often secured complete and primary healing of such grafts, but have not failed to secure eventual healing and a good result by cleanly surgical care of the grafted area and maintenance of a pressure dressing until healing was complete (Fig. 10).

Irradiation dermatitis. If in an area subjected to excessive irradiation multiple keratoses have developed and so close to one another that excision and suture cannot be carried out, the excision of the affected area and its replacement by a whole thickness graft affords a simple solution of the difficulty.

Fig. 14. Crushing injury of left hand, with intermediate and late result of application of pedunculated flap.

If skin over the dorsum of a phalanx is excised and the defect covered with a whole thickness graft from the inner surface of the arm healing can take place so rapidly and perfectly that 6 months later it will be difficult to determine on which finger the graft has been laid (Fig. 11).

If ulceration has already begun we would rarely attempt to use a whole thickness graft but would apply one of intermediate thickness after infection had been controlled as completely as possible by simple cleanly surgical care, immobilization, and pressure dressings.

Recent injuries. If a patient is seen within a few minutes or few hours after sustaining a lacerated wound or avulsion injury with loss of covering tissue, or a crushing injury with destruction of the superficial tissues, and if the patient's condition is such that an immediate cleansing and repair of the wound can be carried out, there is every reason for converting the contaminated wound into a clean wound and closing the wound. These seem to us primary principles of surgical care which are accepted by thoughtful surgeons everywhere.

To cover the raw surface in such a case the application of a whole thickness graft may give the best result attainable (Fig. 12). Obviously one must have a source from which to obtain a graft of suitable size, a raw surface with adequate blood supply, and with sufficient soft tissue still present to afford protection for underlying nerves, tendons, blood vessels, bones, and joints. Under such conditions the graft of whole thickness skin possesses the same advantages that were cited in the paragraphs under "Burn Contractures."

THE PEDUNCULATED FLAP

When structures are laid bare which require for their protection and functional activity a covering of subcutaneous tissue as well as epithelium—structures such as tendons, the larger nerves, and blood vessels—or if the loss is still greater and bones and joints are exposed, the use of a pedunculated flap is imperative. We know of no way of transferring subcutaneous tissue with its overlying skin from one part of the body to another except by maintaining a part of its original

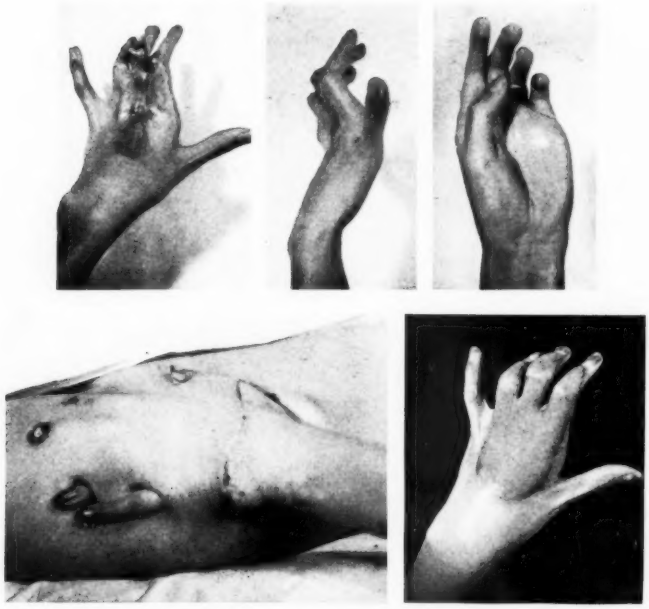

Fig. 15. Mangle burn with result of application of pocket flap and subsequent separation of fingers with aid of whole thickness grafts.

blood supply while new vascular channels between the base and the transplanted tissue are being formed. To cover such raw surfaces on the hand we have come to depend upon two types of flap—the "delayed flap" from the anterior abdominal wall or anterior surface of the thigh, and the "pocket flap" from the same sites. In speaking of a delayed flap we refer to the flap which is prepared for transfer by raising it in one or two stages and which, after it is raised, is immediately returned to its original site and sutured in place (Fig. 13). By permitting a flap to remain at its original site for two or three weeks, as Blair pointed out many years ago in his paper on the delayed transfer of long pedicle flaps, the blood supply entering the flap through its pedicle is stimulated and increased to such an extent that it is possible eventually to incise a fairly long flap along three sides and transfer it to a new site without loss of any portion of the flap. The term "pocket flap" is self-explanatory, but even with this type of flap we prefer if possible to raise a part of the flap and return it to its original site for a period of 12 or 14 days rather than to raise the flap and place the hand underneath it at the primary operation.

The use of the delayed pedunculated flap has many advantages. The flap can be raised under local anesthesia. One can carry the separation of the flap as far as seems advisable and stop short if there is evidence that further elevation at the primary operation would jeopardize its vitality. One can cut the flap of the desired thickness, an important point when one is attempting to secure an extensive thin flap to replace the thin layer of skin and subcutaneous tissue that covers the tendons on the dorsum of the hand. Most important of all, when the flap is ready for transfer, one can incise it along three sides, raise the flap from its bed, cover the raw surface underneath it with a graft of intermediate thickness or by drawing the edges of the defect together with sutures, and attach the flap along practically its entire free border to the edge of the defect on the hand. Such a procedure makes the operation almost a "closed" one, for the only exposed raw surface is the under surface

Fig. 16. (Legend on opposite page.)

of the pedicle as it passes from abdomen or thigh to hand. We have frequently seen such flaps heal by primary union to the edges of the defect on the hand; and with so little inflammatory reaction about the pedicle of the flap that only occasional dressings were required during the 3-week period that is ordinarily allowed for development of the new blood supply to the flap.

Because the pocket flap has a double pedicle and often additional small pedicles between the fingers it can be raised and laid over the raw surface at the primary operation without running serious risk of loss of a part of the flap. Because, however, there is an extensive raw surface exposed to intimate contact with skin surface, where the palm rests on the raw surface underneath the flap, some inflammatory reaction is inevitable, considerable wound discharge results, and when the flap is separated from its attachments to abdomen or thigh a considerable raw surface is left which must still be covered with grafts of intermediate thickness.

In passing, we have not been able to secure healing of the raw surface underneath a pock-

Fig. 16. Complete loss of function of hand following flame burn. Result of application of large pedunculated flap surrounding hand and separating thumb from hand.

et flap by attaching thin grafts, raw surface outward, to the palm before placing the hand underneath such a flap. When this has been attempted the grafts have simply melted away, and no epithelium has remained attached to the raw surface when the pedicles of the flap were divided and the hand lifted away. Furthermore, since we have limited the surgical preparation of the hand to careful and prolonged soap and water cleansing, and have applied no antiseptics to it before it was placed underneath the flap there has been a marked diminution in the amount of wound secretion developing underneath the hand. As a result the care of the wound area has been simplified and preparation of the raw surface for grafting after the hand has been lifted away from the raw surface has required a week or even less, instead of 12 or 14 days.

The chief indications for the use of pedunculated flaps in our experience have been to cover the dorsum of the hand after deep and extensive flame or electrical burns or after injuries in a hot mangle, to secure a covering of normal skin and subcutaneous tissue over the defect left by separating the thumb from the hand, and to replace the covering tissue of hand and forearm after severe infection or crushing injury. Occasionally such flaps have been used after deep chemical burns, after crushing injuries with loss of part of one or more fingers, after removal of a tumor, or after extensive removal of tissue devitalized by excessive radiation. In earlier years a number of cases of burn contracture of the palm were treated by laying the hand underneath a double pedunculated flap taken from the lumbar region. After Blair had demonstrated the possibility of securing more satisfactory results by the simpler method of employing grafts of whole thickness skin, pedunculated flaps have been used rarely for such cases and only in cases with some unusual complication.

Deep burns of the dorsum of the hand (Figs. 14, 15, 16). There is no more difficult problem in connection with the surgery of the hand than restoration of usefulness in a hand in which covering tissues, extensor tendons, periosteum, and dorsal joint capsules have been destroyed more or less completely as the result of a deep burn and the infection which has invariably followed it. A discussion of this entire problem would lead one far beyond the subject of our paper, but it is obvious that the first step toward restoration of function is replacement with normal tissue of the shiny, tense tissue paper-like epithelium which nature left to itself provides as a covering for an extensive raw surface. A satisfactory covering must be flexible so as to permit free movement at the metacarpophalangeal and interphalangeal joints; it must be free from a tendency to contract; and it must be of such a thickness that tendons can be transplanted underneath it at a later date. It is obvious that it would be impossible to transplant tendons underneath a graft of intermediate thickness or a whole thickness graft, even if it were possible to secure healing of such a graft over the deeply denuded dorsum of the hand; yet a visiting surgeon from abroad wrote somewhat disparagingly of the appearance of the pedunculated flaps of some of our patients, as compared with grafts. The fact that these flaps were to serve later both to protect tendon transplants and to make possible their gliding movement had escaped him completely.

In preparing the usual delayed flap for transplantation to the dorsum of the hand it is our custom first to outline the flap by parallel incisions, made if possible parallel to the course of nerves and major blood vessels (Fig. 13). The skin and desired thickness of subcutaneous tissue over the entire area outlined by the parallel incisions are raised at the first operation. All bleeding vessels are ligated with fine silk ligatures; and the flap is sutured with care not to crush or devitalize skin edges. At the end of 10 days the distal end of the flap is cut across; and at the end of another 10 days it should be possible to incise the flap along the healed incisions, divide the subcutaneous tissue at the proper depth to give the desired thickness, and transfer the flap to its new site. Before the flap is actually spread out over the raw surface it is intended to cover, the edges of the defect left by elevation of the flap are approximated with sutures; or, if approximation would produce excessive tension the edges of the defect are drawn inward so as to make the raw surface as small as possible and the remaining raw surface is covered with a graft of intermediate thickness. The hand is then brought underneath the flap and the flap sutured in place over the freshly prepared raw surface.

If the flap is of such size and shape that a relatively narrow pedicle remains as the sole source of blood supply, this pedicle is usually divided completely at the end of 3 weeks and suture of the flap to the hand is completed.

If instead of the type of flap described a pocket flap has been used it may be wise not to detach the entire flap from its original site at one stage. In such cases we have often divided the flap along one side of the hand,—the lower pedicle of an abdominal flap, for example, or the lateral pedicle of a thigh flap—sutured the freed edge of the flap to the hand, and waited for another 8 or 10 days before dividing the remaining attachments.

As indicated above one of the most difficult problems in the reparative treatment of deep burns of the dorsum of the hand is to secure sufficient tissue for restoration of the web. Because of the tendency of the scarred fingers to remain fixed in close adduction it is difficult to hold them abducted underneath a pocket flap and so secure tissue which can eventually be turned down between the fingers to restore the web. We have sometimes met this problem by the use of whole thickness grafts between the fingers after the flap was well healed, as described in the treatment of syndactylism (Fig. 15). Pierce and O'Connor have suggested dividing the distal portion of the flap into strips for the individual fingers and suturing the strips to the fingers at the time the hand is laid underneath the flap. Such a plan would permit some forced abduction of the fingers but would definitely lessen the blood supply passing to the strips over the individual fingers.

Fixed adduction of the thumb. The disability which results from fixed adduction of the

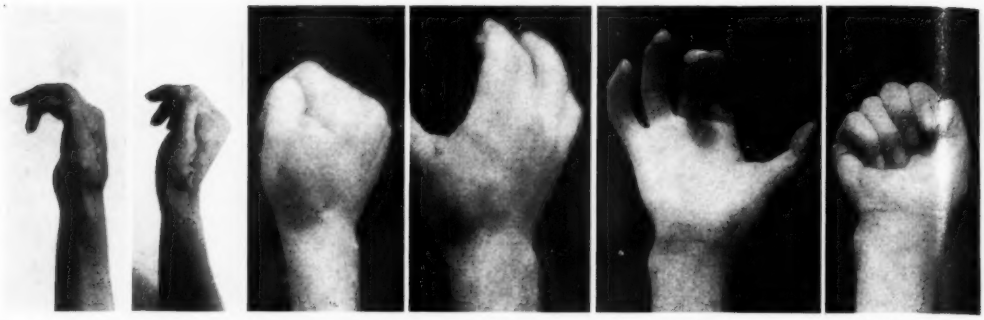

Fig. 17. Fixation of thumb following crushing injury with infection and osteomyelitis; restoration of abduction with aid of a pedunculated flap. Left, before operation; right, after abduction of thumb and covering with flap.

thumb to the hand as a result of burns, crushing injuries with fracture and subsequent osteomyelitis, and long standing infection is even more serious than the inability to rotate the thumb so as to face the fingers. The patient with thenar palsy can abduct the thumb from the hand and hold objects between thumb and forefinger. The patient with a firm scar which fixes the thumb close to the hand can neither abduct the thumb nor rotate it. The disability can be almost as serious as that due to loss of the thumb.

The use of a delayed pedunculated flap from the lower abdominal wall is almost an ideal solution of this problem. With the aid of an elongated flap, prepared as described above, the operation can be made practically a closed procedure throughout, the thumb separated from the hand in such a way as to restore the normal span between thumb and index finger, and the resulting defect immediately covered with the prepared flap of normal skin and subcutaneous tissue (Fig. 17).

Extensive scar contractures of hand and forearm. With extensive loss of the covering tissue of the forearm as well as the hand the operation must be planned on a large scale if a satisfactory result is to be accomplished. Here again the principle of the delayed transfer of a flap, careful immobilization to avoid tension on the pedicle, patience that permits the development of an adequate blood supply, and perhaps division of the attachments of the flap in two stages provide safeguards against loss of transplanted tissue and perhaps failure and bitter disappointment.

For covering an extensive area the elongated flap with a relatively narrow pedicle may not provide sufficient tissue. It may be preferable in such a case to raise an apron-like flap with a broad pedicle, to content oneself with covering a part of the involved area at the primary transfer and subsequently to use the pedicle and the tissue adjoining it to complete the procedure (Fig. 19).

In such a case the principle of preparing the flap and undermining it is utilized both before the flap is first attached to hand and forearm, and again before the pedicle is separated from the abdominal wall. If one is attempting, for example, to wrap a flap of skin and subcutaneous tissue about the entire forearm, after the first stage is completed and the tissue first transplanted has healed kindly the area above the site of attachment of the broad pedicle is undermined without cutting into the exposed pedicle at any point and then returned to its bed for a period of 10 or 12 days. In other words, the remaining tissue which is finally to be separated and transplanted is prepared by a preliminary elevation and immediate replacement so as to stimulate the newly forming blood supply from hand to flap, that it may eventually be adequate to maintain the nutrition of the large flap, a part of which served as the pedicle of the tissue first transplanted (Fig. 19).

We know of no hard and fast rules that one can make with reference to time periods. Much depends on freedom from infection and the rapidity with which incisions heal. In case of doubt it is surely wiser to delay a few

Fig. 18. Result of application of pedunculated flap after excision of malignant ulcer recurring after 3 operations and prolonged irradiation during a period of 16 years.

days or a week than risk the loss of tissue which is essential for success.

COMBINED METHODS

The advantages of covering raw surfaces at the earliest possible moment that it can be accomplished with safety to the patient, and the unsatisfactory character, from the standpoint both of appearance and function, of the epithelium which forms spontaneously over a large raw surface have been referred to above and have been stressed by practically everyone who is seriously interested in the problem of covering raw surfaces. A combination of methods—early application of a graft of intermediate thickness, followed at a later date by its replacement with a graft of whole thickness skin or a pedunculated flap—may in certain cases offer the best method of securing a satisfactory result. Frequently, as Brown has pointed out, the results of early application over a raw surface of a graft of intermediate thickness are so satisfactory that the second operation is not required.

An unusual example of the opportunity to utilize a combination of methods is that of the "degloved hand," in which all the covering tissue has been torn from hand and fingers in an avulsing, crushing injury. In one such case which came under our care a few hours after the injury was sustained it was possible to lay two large grafts of intermediate thickness over the palm, and after the grafts were sutured in place to lay the hand, with the palm thus covered, under a pocket flap raised from the anterior surface of the thigh.

Although we attempted to abduct the thumb well away from the hand and to help hold it in such a position by bringing the tip of the thumb through a separate opening on the thigh and to separate what remained of the fingers in the same manner, a constant tendency to draw the hand upward out of the pocket resulted in enough retraction to free the thumb and fingers underneath the flap. The constant contraction of the adductor of the thumb and of the interossei gradually drew the thumb and fingers together underneath the flap. The raw surfaces thus brought into contact became completely fused. Our problem now is to separate the thumb from the hand and the fingers from one another in the effort to secure some restoration of function of the individual digits.

THE TUBED FLAP

Much has been written about the tubed flap; and it has definite advantages when one wishes to transplant skin and subcutaneous tissue, for example, from the abdominal wall to the front of the neck or face. We no longer use it in transplanting skin and subcutaneous

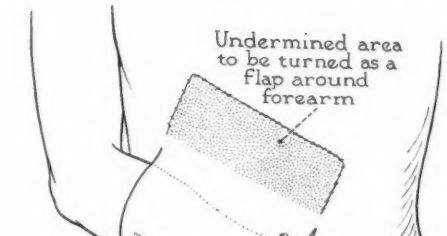
Undermined area to be turned as a flap around forearm
Abd. wall covered with healed grafts
Line of primary attachment of flap.

Fig. 19. Plan of procedure for surrounding entire forearm with a flap of skin and subcutaneous tissue. The principle of delayed transfer is utilized both with the primary flap already attached and the part to be last applied.

tissue as a permanent covering for the hand. Its disadvantages are many. Considerable time is required during the operation to fashion the flap into a tube. If a tube is formed one must determine the amount of subcutaneous tissue raised with the skin by the tension it produces on the skin edges while the tube is being closed rather than by the desired thickness. If the tube is closed with only a little excess of tension the sutures may cut through the skin and wide separation of the edges take place. Such a complication may cause long delay in healing, and completely jeopardize the success of the procedure. Finally when the tube is reopened the scar along the line of closure must be excised with some sacrifice of tissue, and one may find it exceedingly difficult to leave a uniform layer of subcutaneous tissue over the entire surface of the flap. Because of these disadvantages we prefer to use a flap which is prepared in two stages, but left spread out over its original site during the period allowed for the compensatory increase of the blood supply brought to the flap through its pedicle.

SUMMARY OF CASES

Many men question the value of all statistical reports, and the cynical reader may

TABLE I.—CAUSE OF DEFECT AND TYPE OF OPERATION CARRIED OUT

	Flame and mangle burns	Irradiation burns	Electrical burns	Crushing injury	Injury, followed by infection	Congenital deformities	Dupuytren's contraction	Tumors	Total
Graft of intermediate thickness	19	11	2	29	15	1	..	..	77
Whole thickness graft	88	8	6	32	19	25	40	9	227
Pedunculated flap	40	7	7	29	36	3	..	5	127
Total	147	26	15	90	70	29	40	14	431

sometimes wonder that men with ample opportunity and abundant material do not achieve still more satisfactory results. The following statistics are reported to indicate the relative indications and usefulness of different types of grafts and flaps and the change in methods that has taken place with increasing experience. If the cases shown in Table I were grouped by years the tabulation would show that for a number of years no pedunculated flaps have been used to cover the palm and fingers except in cases of firm adduction of thumb to hand, and that the only flaps which have been raised and transferred to the hand at the primary operation have been pocket flaps, almost always from the anterior surface of the thigh. With increasing experience the indications for the use of grafts of whole thickness and of intermediate thickness have been constantly widened, particularly in cases of burns and injuries involving the palm. As a result time has been saved for the patient and better results have been secured both from the standpoint of function and appearance.

During a period of 20 years, the first 10 in association with Dr. Allen B. Kanavel and the past 15 in association with Dr. Michael Mason, there have been under our care 431 patients with injuries of the hand and forearm which required some form of graft or flap for replacement of destroyed covering tissues. In 147 cases the defect resulted from flame or mangle burns, in 90 cases from crushing injuries, in 70 cases from extensive injury followed by infection. Other causes included x-ray and radium burns, electrical

burns, congenital deformities, tumors, and involvement of the skin in contractures of the palmar fascia (Table I).

In 77 cases grafts of intermediate thickness were used, in 227 whole thickness grafts, in 127 some form of pedunculated flap. Of the third group in 57 cases a flap was laid over the raw surface at the primary operation; in 70 a delayed flap was used. Of the third group a pocket flap was used in 15 cases, in 9 without preliminary elevation of the flap. In 22 patients, 4 in group 1, 11 in group 2, 7 in group 3, bilateral involvement was present which required similar treatment in both hands. In many cases several types of graft were required at different stages, for example, whole thickness grafts to separate fingers fused in an acquired syndactylism after a flap of skin and subcutaneous tissue had been applied to cover an extensive dorsal defect; and in 5 cases all three types of graft were used at some stage of the treatment. Some of the results obtained, neither the poorest nor the most satisfactory, are illustrated in the preceding pages.

SUMMARY

The various types of graft and flap that we have found most satisfactory in covering defects of the hand and forearm have been described; and the principles involved in their use and application detailed as exactly as possible.

The graft of intermediate thickness, of whole thickness skin and the delayed flap raised from anterior surface of abdomen and thigh meet nearly all the indications encountered, and in our hands have proved useful in providing a resistant and permanent covering which in the majority of cases has proved satisfactory from the standpoint of appearance and function.

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THE PROBLEM OF HYPOPROTEINEMIA IN SURGICAL PATIENTS

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CLINICALLY, hypoproteinemia is observed in a variety of conditions. Among those of special interest to the surgeon are: chronic gastro-intestinal diseases, such as peptic ulcer, ulcerative colitis, or regional enteritis; pancreatic, biliary or intestinal fistulas; chronic suppurative diseases including lung abscesses and pyarthrosis; acute appendicitis; and malnutrition and cachexia resulting from carcinoma. One is usually able, in these cases, to attribute the deficiency in serum proteins to one of several mechanisms: (1) diminished intake of food due to anorexia, vomiting, or dietary restrictions; (2) deficient absorption of nutritive elements from ingested food because of alterations in the mucosa of the intestinal tract or a deficiency in accessory food factors; (3) severe diarrhea; (4) loss of large amounts of body fluid (plasma) in extensive burns or profuse drainage from an abscess; (5) decrease in the amount of absorptive area of the intestine because of operative procedures (resection or short-circuiting).

In the experimental laboratory, hypoproteinemia can be induced easily by one of two methods: (1) plasmapheresis or (2) restriction of dietary proteins. Furthermore, the deficiency of plasma protein thus induced can be remedied by supplying excess protein, either orally or parenterally (20, 30, 31, 32, 34, 16, 19). On the basis of this work and many clinical observations, the "loss and lack" theory of the pathogenesis of hypoproteinemia was formulated. This theory postulates that hypoproteinemia is due either to a deficiency in protein intake, or to an excessive loss of protein through one of the routes mentioned above, or through the urine. If this is correct, the problem of hypoproteinemia, particulary in relation to therapy, is greatly simplified. However, certain facts have been determined which cast considerable doubt on the adequacy of the "loss and lack" theory.

Two problems are presented in the consideration of the pathogenesis of hypoproteinemia. First, does the "loss and lack" theory explain all the manifestations of hypoproteinemia or is there evidence pointing to the presence of a specific mechanism concerned in the production of plasma proteins, and second, is there an equilibrium between the plasma proteins and tissue proteins so that one may replace the other in times of stress.

In relation to the first, Bloomfield in 1934, on the basis of experimental work in rats, suggested that the "loss and lack" theory was inadequate to explain all the variations in serum protein deficiency and regeneration and suggested that a specific mechanism might be responsible for these variations. He makes the following statement:

"The question may be raised, however, whether such a single concept (loss and lack) fits all the facts of clinical and experimental experience and whether one must not postulate in addition some injury to, defect of, or inadequacy of the blood protein-forming mechanism as an accessory if not a primary difficulty; in point of fact, the evidence for the 'loss and lack' theory when inspected from this angle reveals a number of serious breeches. . . ."

This view is upheld by such outstanding workers in this field, as Melnick and Cowgill (20) Weech and his co-workers (30, 31, 32, 34) and Bing. The evidence in support of this theory is summarized briefly in the following paragraphs.

1. There is experimental evidence that loss of tissue protein and plasma proteins do not parallel one another and the maintenance of the serum protein concentration bears no relation to the nitrogen metabolism of the organism as a whole. Also, dogs may utilize dietary

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protein to satisfy the nitrogen requirements of the body without adequate serum protein regeneration.

2. Animals exhibit an amazing ability to regenerate serum proteins even when subject to repeated plasmapheresis. Patients likewise form serum protein easily. Therefore, protein loss, in order effectively to lower the concentration of plasma proteins, must be accompanied by a defect or impairment in the blood-protein forming mechanism, or else the plasma protein would be rapidly restored.

3. With marked loss of protein, the serum proteins do not continue to fall but maintain themselves at a constant low level. While some experimenters believe that this is accomplished by drawing on reserve protein stores, there is ample evidence that this leveling process will occur after these stores have been exhausted. This, in turn, points to the presence of a controlling mechanism.

4. There is no relationship between the initial nutritional state of dogs and the development of hypoproteinemia after plasmapheresis.

5. In Bright's disease there is no constant relation between the loss of protein in the urine and the reduction in the serum proteins. After prolonged proteinuria the serum proteins become established at a constant low level.

6. Certain infections can depress the ability of the body to regenerate serum proteins, even if ample or excessive protein is made available. This has been shown experimentally as a result of turpentine abscesses and has been observed clinically by Bruchman, D'Esopo, and Peters. We have observed this phenomenon in acute appendicitis several times. Patients who are apparently in normal nutritional status may develop a deficiency of the serum proteins very quickly following fulminating appendiceal infections.

7. In Bright's disease, a high protein diet has no appreciable effect on the concentration of the serum proteins regardless of whether there is a positive or negative nitrogen balance (1, 22).

8. There is some evidence that malnutrition may cause hypoproteinemia because of damage to the regenerative mechanism rather than as a result of a restricted protein intake.

9. In severe liver disease, the ability to regenerate serum proteins may be lost although an excess of proteins is being administered. We recently treated a case of acute yellow atrophy of the liver in which the serum proteins fell to a seriously low level and remained there in spite of a diet very rich in protein and daily blood transfusions.

On the basis of the clinical and experimental evidence adduced in the preceding paragraphs one must conclude that there is undoubtedly a specific mechanism which controls the formation of serum proteins. This is of great importance in therapy, for if this mechanism is impaired it is obviously futile to administer large amounts of proteins which cannot be utilized to regenerate serum proteins. This may explain the failure, clinically, to restore proteins to normal even though all routes of administration are employed, and the amounts ingested are sufficient. In connection with this the second question raised assumes importance. If there is a reciprocal equilibrium between tissue and plasma proteins then one can draw from the other in times of stress. Holman, Maloney, and Whipple state that there is a "dynamic equilibrium between tissue proteins and plasma proteins which is governed by the physiological needs of the moment." While this is true to a certain extent, it does not mean that tissue proteins or the products of tissue protein catabolism can be utilized to form new serum proteins. However, the reverse of this reaction, namely, the conversion of plasma proteins into tissue proteins can and does occur. Undoubtedly there are certain reserves from which serum proteins can be regenerated, but once these are exhausted, no further aid may be expected from the tissue proteins. Whipple describes three types of tissue proteins: (1) the labile reserve protein which is readily available for serum protein regeneration, (2) the dispensable reserve protein which is less readily available, and (3) the indispensable and fixed protein of the body cells which is never available. This division makes available a certain amount of reserve protein, but when this is exhausted, the serum proteins can no longer draw on the tissues for replenishment. Thus, although the plasma protein does contribute to the protein needs

of the body cells and an animal can be kept in nitrogen equilibrium and weight equilibrium by the administration of proteins intravenously and carbohydrates and fat by mouth, the body proteins contribute only with difficulty to the plasma protein. This has been summarized by Pommerente, Slavin, Karchen and Whipple as follows: "In an emergency the plasma proteins may contribute to body proteins but the current will not flow easily in the opposite direction and the body proteins may be said to stand by helpless to aid while vital plasma proteins are depleted even to a lethal point. . . . Evidently in this emergency the plasma protein is very largely, if not wholly, dependent on materials coming in from the gastro-intestinal tract."

Recent evidence has tended to implicate the liver as an important, if not the specific, mechanism concerned with serum protein regeneration. Whether this is confined to the liver or to the entire reticulo-endothelial system is still a moot point. Whipple points out that the liver participates in the "assembly of amino-acids and other constituents of body proteins into aggregates which may be used in the liver or elsewhere to form specific proteins of the body cells." Weech suggests that liver disease interferes with regeneration of serum proteins and believes that the liver may be affected in prolonged malnutrition so that return to normal of the serum proteins is markedly delayed even when adequate feedings are resumed. Johansen reports hypoproteinemia in cases of liver disease and expresses the opinion that the liver assumes a rôle of major importance in the synthesis of proteins. Many workers have called attention to the damage sustained by the liver as a result of surgery and anesthesia, particularly in cases of the hepatorenal syndrome. It is possible that lesser degrees of damage may be responsible for the hypoproteinemia which is occasionally encountered in surgical cases and which is so resistant to treatment by replacement therapy.

RELATIONSHIP BETWEEN PLASMA PROTEINS AND EDEMA

It has been established by experimental and clinical evidence that the plasma proteins are the dominating factor in the distribution of extracellular fluid. Starling in 1898 first postulated that the movement of fluid between the vascular channels and the interstitial spaces is governed by two factors: (1) the capillary blood pressure, and (2) the colloidal osmotic pressure of the blood. The former tends to force fluids into the tissues while the latter draws fluid from the interstitial spaces into the blood stream. He emphasized the rôle of the plasma proteins in this interchange. The colloid osmotic tension which is largely determined by the concentration of plasma proteins counterbalances the mechanical effect of the hydraulic pressure in the capillaries (the capillary blood pressure). The proteins, to which the vascular walls are normally impermeable, produce an osmotic pressure difference between the serum and the relatively protein-free interstitial fluid with which they are in diffusion equilibrium and this is sufficient to counterbalance the effect of the capillary blood pressure. In health this oncotic pressure is greater than the mean capillary pressure and will absorb any excess of fluid in the tissue spaces (14, 15). Krogh postulates that there is thus a "margin of safety" which keeps the fluid in the vascular channels and the interstitial fluid in equilibrium and prevents edema.

According to this theory, edema will develop when the oncotic pressure is low, in relation to the capillary blood pressure, and this may occur as a result of one of the following: (1) loss of serum proteins, (2) increase in capillary pressure as in venous obstruction, or (3) the vessel walls become pervious to proteins as in inflammatory states or vasomotor paralysis (22). Recent work, however, has demonstrated that the mechanical forces of the interstitial tissues must be considered in the production of edema. These forces consist of two factors: (1) the oncotic pressure of the tissue fluids based on the protein content, which, however, is very low in filtration edema fluid and therefore is of little significance, and (2) the tissue tension or elasticity (26). Weech and his co-workers (30, 31, 32, 34) suggest, as a result of their studies that there is no definite critical level of the serum proteins for the production of edema, but rather a "correlation level" which pertains to that

concentration of the serum protein which is first found in association with clinical edema. They state:

"The critical level of protein in the serum is determined by that concentration which permits the attainment in the tissue spaces of mechanical pressures great enough to break down the restraining action of the connective tissue boundaries of the spaces. Obviously such pressures can occur only when the colloid osmotic pressure of the serum has fallen below the capillary blood pressure, but the effect of the fall on pressure outside the capillaries is more directly the cause of edema than the disturbance of the balance between the internal forces."

This factor of tissue elasticity is of importance for the reason that with increasing stress on the tissues as a result of declining serum proteins, there is expansion of the intracellular space for some time prior to the appearance of edema. When the stress becomes too great, that is, when it overcomes the elastic strength of the tissue framework, the tissues seem to be torn apart and palpable edema results.

We may then state that edema is a result of a disturbance in the balance between two forces. On one side there is the colloid osmotic pressure of the blood less that of the tissue fluid, and on the other, the effect of the hydraulic pressure of the capillary blood pressure, less the pressure due to the elasticity of the tissue spaces. This concept enables us to explain many vagaries in the appearance of edema. It is well known that no actual critical level for edema is universally present. Edema may occur in some cases at a concentration of 6 grams per cent of serum protein and be absent in other cases at a level for the proteins of 5 grams per cent. It is also well known that there are certain sites of predilection for the appearance of edema, and these are in the soft, elastic, subcutaneous space. Finally, the effect of physical activity on the pressure in the tissue spaces may influence the appearance of edema. These phenomena can best be explained by the theory outlined above.

The principal constituents of the serum proteins are the albumin and globulin fractions. The normal range for the serum albumin is from 3.5 to 5.0 grams per cent, while for the globulin fraction the range is from 1.5 to 2.6 grams per cent. The albumin and globulin have no chemical similarity and bear no quantitative relationship to each other. There is actually no significance to the albumin-globulin ratio inasmuch as each is affected by different conditions and the concentration of one constituent in the plasma has no effect on the concentration of the other. Serum-globulin may be increased in the chronic infections, syphilis, lymphogranuloma venereum, and tuberculosis. Albumin is diminished in cases of malnutrition and extensive loss of serum protein. In patients with hypoproteinemia the globulin concentration is not commonly decreased, while the albumin fraction is very low. Govaerts (8, 9) estimated the osmotic pressure of serum albumin and globulin independently. He determined that the osmotic pressure of albumin is 5.5 millimeters of mercury for every 1 gram per 100 cubic centimeters while that of globulin is only 1.4 millimeters of mercury for every gram per 100 cubic centimeters. Accordingly the total oncotic pressure of normal serum varies from 21 to 29 millimeters of mercury per 100 cubic centimeters. This explains the importance of lowered albumin concentration in the production of edema, and the relative insignificance of variations in the globulin content. While a decrease of 2 grams per cent of albumin would lower the oncotic pressure of the blood approximately 11 millimeters of mercury a similar change in globulin would mean a decrease of only 2.8 millimeters of mercury. Palpable edema will almost invariably be present when the albumin fraction falls below 2.5 grams per 100 cubic centimeters and is rarely found when concentration of this fraction is over 3 grams per 100 cubic centimeters. With these values for albumin, the globulin may be normal, increased, or decreased but the effect on edema will be insignificant. Various authors (21, 13, 33), state that edema will occur at levels for the total serum proteins of 5.5 ± 0.3 grams per 100 cubic centimeters but as has been shown, the figures which are presented are susceptible to definite fluctuations.

RELATIONSHIP BETWEEN PLASMA PROTEINS AND OTHER FACTORS RESPONSIBLE FOR EDEMA

It is well known that the distribution of body fluids is affected by many factors. While the serum proteins are among the most important, the rôle of the electrolytes should not be underestimated. Variations in the character, concentration, and distribution of the acid and base electrolytes will cause marked changes in the hydration of the human body. In the healthy subject, an excess of sodium chloride ingested through the gastro-intestinal tract will be promptly excreted by the kidneys. If a sufficiently large excess of salt is ingested and the fluid intake controlled, dehydration of varying severity will be induced by the excretion of the excess salt in solution, thus the body fluids will be depleted. If, however, the kidney is diseased or its function impaired as it is so frequently in the seriously ill surgical patients, salt given in excess will be retained in the body and will cause the retention of water in an effort to maintain the proper electrolyte concentration of the body fluids. As a result of this mechanism by which the electrolyte concentration is protected from excessive fluctuation, edema is produced. This edema will also be adversely affected by hypoproteinemia if this should be present. On the other hand, hypoproteinemia existing in conjunction with dehydration may not cause edema, regardless of the degree of the deficiency because retention of fluid in these cases would seriously interfere with the concentration of electrolytes.

In patients who, because of vomiting, diarrhea, or other causes, have had an excessive loss of electrolytes, this same protective mechanism will result in loss of body fluids until the correct concentration of electrolytes in the body fluids is established. Hemoconcentration and dehydration are the sequelæ of this chain of events. Hemoconcentration, as determined by studies of the hematocrit and specific gravity values will alter the values for all blood constituents. A patient who is dehydrated may show a serum protein value of 7.0 grams per 100 cubic centimeters or over. However, when sufficient fluid and salt are administered to overcome the dehydration the true value for the proteins can be determined and this may be definitely below edema levels. Edema will then result and if one has not carefully considered the changing relationships of plasma proteins, blood concentration, and electrolytes, this edema may be attributed erroneously to excessive salt administration. It is of the utmost importance therefore, in administrating fluid to sick surgical patients to evaluate carefully the aforementioned factors. The amount of fluid to be administered can be determined by studies of the specific gravity of the blood and the hematocrit, while the character of the fluid to be given (i.e., saline, distilled water, whole blood, or plasma) can be determined by studies of the plasma chlorides and plasma proteins.

CLINICAL MANIFESTATIONS OF HYPOPROTEINEMIA

The clinical manifestations of hypoproteinemia are chiefly dependent on the alterations in the fluid distribution of the body which are induced by this state. Various organs may be affected, giving rise to what may appear to be dissociated symptom complexes. These symptoms and signs, however, are simply the external and palpable evidence of a profound physiological and nutritional disturbance. Reduction of the total serum protein below 3 grams per 100 cubic centimeters is usually considered to be incompatible with life. In the range between this figure and the normal, various disturbances are observed. Often, the severity of the clinical picture does not parallel the reduction in serum proteins and marked disturbances are noted with but slight variations in the proteins. In addition various other factors may influence the clinical picture. Disturbances in the nutritional state as a result of avitaminosis or dehydration profoundly affect the signs and symptoms caused by hypoproteinemia. For example, a deficiency of vitamin B complex may augment the inhibitory effects of diminished serum proteins on the intestinal tract, while lack of salt or dehydration may delay the appearance of edema. In a consideration of nutritional disturbances all factors must be thoroughly evaluated.

The effects of hypoproteinemia may be divided conveniently into four categories:

(1) the production of peripheral edema; (2) the production of visceral edema, and particularly pulmonary edema; (3) the inhibition of gastro-intestinal activity; and (4) the inhibition of wound healing. Frequently all of these are noted in the same patient.

Peripheral edema. This is usually the earliest and most frequent manifestation of hypoproteinemia. There are certain sites of predilection for this edema, notably in the loose areolar tissue of the subcutaneous spaces. The abdominal wall, the back of the ankle, the legs, and the face are the common sites. It is this symptom which, as a rule, calls the attention of the surgeon to the deficiency which exists in the concentration of the serum proteins, and while not in itself a serious complication, it forewarns of others far more serious. It indicates a severe nutritional disturbance which may not be confined to the blood, and which requires intensive treatment. As pointed out previously, the normal human regenerates serum protein with amazing rapidity so that when a deficiency exists and is manifested by the early signs of fluid unbalance, one must consider not only whether nutrition is disturbed but whether the mechanism for regenerating protein has been impaired. Occasionally the occurrence of peripheral edema causes no change in the general attitude or reaction of the patient. We have observed, however, that most patients react unfavorably to this development. They are frequently irritable and restless, and may have anorexia, nausea, and vomiting. Rarely they may become irrational. A typical case report is presented.

CASE 1. E. Z., hospital No. 69224. A 6 year old white child was admitted to the service of Dr. M. Bodenheimer on February 28, 1938. She had been severely burned by a gas stove. Examination revealed extensive second degree burns of the right arm, forearm, hand, and the posterior aspects of the right arm and leg, both buttocks, and the back. After a preliminary cleansing of the burned areas, she was treated by the tannic acid-silver nitrate method. Fluids were administered parenterally. On admission, marked evidence of hemoconcentration was present. Examination of the blood revealed 16 grams per cent of hemoglobin and a red blood cell count of 6,400,000 per cubic millimeter. In about 1 week, after fluid balance had been restored, the hemoglobin estimation showed 11.8 grams per cent and the red blood count was 4,960,000 cells. The patient reacted well to the local therapy, but on March 3, 3 days after admission, her serum proteins totalled only 5.3 grams per 100 cubic centimeters. The albumin fraction was 3.5 grams per cent and the globulin 1.8 grams per cent. The following day, peripheral edema appeared involving the back, neck, face, and extremities. The child was placed on a high protein diet and given glycolixir tablets by mouth. In addition repeated transfusions were administered. Table I summarizes the further course:

It is evident from this case that several factors were involved in the protein depletion. Initially, loss of fluid and plasma from the burned areas caused marked hemoconcentration and initial depletion of the plasma proteins. The hemoconcentration was controlled by the administration of sufficient fluid and electrolytes as evidenced by the drop in hemoglobin from 16 grams to 11 grams per 100 cubic centimeters in 2 days. During this time, in spite of high protein diet and several transfusions, the serum protein remained low. When the initial infection was controlled the serum proteins returned to almost normal figures. Then when the serious secondary infection occurred, the serum protein concentration again fell and edema recurred. Intensive administration of protein during this period had no effect on the falling proteins of the serum, indicating that regeneration was not taking place. During this

TABLE I.—SUBSEQUENT COURSE IN CASE 1

Date	Serum proteins gm. %			Hb. gm %	R.B.C. million	Course
	Alb.	Glob.	Tot.			
3–7	2.7	1.3	4.	11.8	4.96	Edema still present. Anorexia, irritability
3–14	2.7	2.6	5.3	11	4.00	Edema subsiding. Infection under eschar
4–20	3.6	2.5	6.1	10.4	3.84	Infection under control. No edema. General condition much improved. Thiersch grafts on 4–30–38
6–1	2.8	2.8	5.6	7	2.81	Infection recurred. Granulations very sluggish. Child is very toxic. Transfusions given repeatedly.
6–6	2.8	2.8	5.6			Slight peripheral edema. Unchanged
6–27	4.4	3.2	7.6	12	4.22	Much improved. No infection
7–8	4.5	2.9	8.4	10.2	3.74	Much improved. Additional Thiersch grafts on 7–2 taking well

latter interval a severe secondary anemia and infection were present. It is conceivable that because of the anemia and infection sufficient damage to the blood forming mechanism took place (in the liver?) to render it unable to utilize the proteins administered through the gastro-intestinal tract. During this period of hypoproteinemia the granulating areas were edematous and epithelialization was almost absent. Finally, when the infection responded to treatment both the hemoglobin and the proteins returned to normal.

The striking point in the progress of this patient was the parallelism between the general condition and the presence or absence of edema. When edema was present the child was irritable, apprehensive, and feeding had to be forced. With an improvement in her serum proteins (and, incidentally, in her hemoglobin values), the entire picture changed and she became more alert and seemed generally improved. We have noted this in other cases, and while we have not been able to elicit definite neurological signs of any significance in these cases, we have speculated on the possibility of the presence of some cerebral edema.

Visceral edema. In this category we are primarily interested in pulmonary edema. Jones and Eaton have pointed out that the edema resulting from hypoproteinemia frequently involves the parenchymatous organs, and they reported 5 cases of pulmonary edema, one of which ended fatally, as a result of hypoproteinemia. Apparently the lung is one of the sites of predilection for edema in these cases.

We have observed this complication several times and believe that it occurs much more frequently than it is recognized. Pulmonary complications occurring in the postoperative course are usually diagnosed as atelectasis or pneumonia but frequently neither the course nor the roentgenographic examination confirms this diagnosis.

Transient pulmonary edema of a mild grade may simulate a pneumonic process and may be incorrectly diagnosed if the true nature of the causative factor is not recognized. Occasionally the edema of the lungs may occur very quickly and be the direct cause of death, even though no cardiac decompensation is present.

It is a debatable point whether pulmonary edema can be caused by the excessive administration of fluids without excess of salt in the postoperative period. Undoubtedly when cardiac decompensation is present pulmonary edema may occur as a result of right-heart failure. In the absence of cardiac weakness it is unlikely that pulmonary edema will result from over-administration of fluids unless sodium chloride in great excess is likewise administered or hypoproteinemia is present. As a matter of fact, administration of glucose in distilled water may have a dehydrating effect on the body. Glucose even though administered in an isotonic (5 per cent) solution does not act in the same manner as salt solution in retaining fluids in the body. The glucose is metabolized leaving distilled water which is excreted with some of the body salt in the urine and in this way causes a loss of interstitial water to maintain the electrolyte concentration at normal (7). In those cases in which fluid has been pushed to the point of water intoxication cerebral edema will occur and cause death but pulmonary edema is not marked. While indiscriminate administration of fluid is to be condemned strongly, it often becomes necessary to administer from 4000 to 5000 cubic centimeters in one 24 hour period to restore the salt and water balance of a patient. Occasionally a surgeon may hesitate to administer this amount because of the erroneous assumption that it will cause pulmonary edema. This fear, as has been pointed out above, is entirely without foundation if the cardiac status is good. The real dangers of dehydration are far more important than the fancied ones of water-logging, but if fluid is administered according to a rational method, neither of these should occur.

In patients with hypoproteinemia, on the other hand, pulmonary edema can occur with the administration of minimal amounts of fluid and even though the patient is in negative water balance. In contrast to the parenchymatous edema resulting from water intoxication, the edema resulting from hypoproteinemia frequently involves the lungs. In the following case the pulmonary edema was considered largely contributory to the lethal outcome.

CASE 2. F. E., Hospital No. 80006, was admitted on November 11, 1939, with signs and symptoms of acute appendicitis. Laparotomy was performed immediately and a perforated gangrenous appendix was removed. There was a moderate amount of free, purulent fluid in the peritoneal cavity. The wound was drained and closed in layers. The patient developed a severe grade of paralytic ileus which was treated with a Miller-Abbott tube. On the fifth day after operation mild peripheral edema was observed, and on the following day the serum protein concentration was 5.4 grams per 100 cubic centimeters. Two days later complete dehiscence of the abdominal wound occurred without obvious signs of infection. This almost characteristic manifestation of the hypoproteinemic state will be considered in connection with another case. Several transfusions were given but the edema persisted and the patient became progressively more toxic. The salt and fluid balance was carefully watched and because of the edema, the patient was kept slightly below a positive balance. In spite of these precautions the serum proteins showed no improvement and on November 24, 1939 the concentration was still 5.4 grams per cent. On the fourteenth day after operation sudden pulmonary edema developed which did not respond to oxygen therapy or transfusions. There were no signs of heart failure. The edema progressed and peripheral edema became more marked until death of the patient ensued 2 days later.

Disturbances of gastro-intestinal motility. Hypoproteinemia exerts a definite inhibitory effect on the motility of the gastro-intestinal tract. This has been observed in dogs by Mecray and his associates who found that an increase in the gastric emptying time accompanied hypoproteinemia. This occurred in dogs with intact stomachs and in those upon whom short-circuiting operations had been performed. Clinically, this phenomenon has been observed repeatedly. Jones and Eaton reported a case of fatal intestinal obstruction in a patient with hypoproteinemia and others have detected obstructions of varying degrees. We observed a patient who, immediately after a subtotal gastrectomy for ulcer, developed all the signs of an upper intestinal obstruction. Laparotomy revealed thickened and edematous loops of bowel with edema at the gastro-enterostomy stoma. No other obstructive mechanism was found. Unfortunately no studies of the serum proteins were made but in view of our experience in subsequent cases we feel that this was definitely a result of hypoproteinemia.

Frequently, it is found that persistent vomiting will occur after gastro-enterostomy or operation on the bowel. Inasmuch as these patients are in a poor nutritional state, hypoproteinemia develops quickly following operative procedures, and particularly after those which necessitate abstinence from oral feeding. This leads to edema of the stoma and the intestinal wall and a picture resembling acute obstruction develops. Roentgenographic examination is of little value as it merely confirms the presence of obstruction without demonstrating the etiological factor. Whether the obstruction or diminished motility is due entirely to the edema of the stoma with consequent narrowing or to edema of the entire thickness and extent of the gastric and intestinal wall which interferes with effective muscular contraction is debatable. Mecray, Borden, and Ravdin believe the former to be true on the basis of fluoroscopic examination of dogs following a barium meal. They found that, while motility was almost absent in hypoproteinemic dogs, intestinal peristalsis and tone were normal.

When the serum proteins are restored to normal the obstructive symptoms quickly subside and the clinical improvement of the patient is marked. This is further evidence of the importance of the proteins in causing this complication. Inasmuch as these patients are poorly nourished they frequently present vitamin deficiencies which augment the effect of the hypoproteinemia on gastric motility. This is particularly true of vitamin B, which therefore, should be administered in conjunction with proteins. Recently Stengel and Ravdin have suggested the use of the Miller-Abbott tube for feeding purposes following gastric or intestinal operations. The end of the tube is pulled through the stoma and feeding of proteins is started immediately following the operation. This is well tolerated and is effective in aiding the restoration of proteins in the serum.

Case report. M. M. M., No. 72350, a white male, 54 years of age, was operated upon for a carcinoma of the stomach and a Pólya type of gastrojejunostomy performed on September 9, 1938. His preoperative status was good and he was considered a good operative risk inasmuch as his symptoms had been present for only 4 months and he had been

eating well. His blood chemistry before operation was normal; the hemoglobin was 13 grams per 100 cubic centimeters, the red blood cells numbered 4,640,000 per cubic millimeter. Following the operation vomiting commenced and was persistent. Wangensteen suction was instituted on the second day after operation and was continued for 3 days. Vomiting persisted and on the thirteenth day peripheral edema of the extremities was noted. At this time the patient was dehydrated and the total proteins of the serum were 6.1 grams per 100 cubic centimeters. We felt that this value was misleading because of hemoconcentration and instituted a high protein diet. Roentgenogram revealed no small intestinal obstruction. The high protein diet of easily assimilable materials was continued through an indwelling tube but on the eighteenth day after operation the serum proteins were reduced to 5.1 grams per 100 cubic centimeters which we took to be a truer index because hydration had been accomplished by this time. Proteins were pushed and 3 days later vomiting had completely ceased. When the vomiting stopped the serum proteins had been increased to 5.7 grams per 100 cubic centimeters which although low, was apparently above the edema level. The remainder of the course was uneventful.

This case illustrates two very important factors. In the first place, estimation of total serum proteins must be done in conjunction with studies of blood concentration. We now routinely do hemotocrit studies in order to judge hemoconcentration more accurately. The McLure Aldrich test for dehydration has not been sufficiently accurate in a very small series of cases in our hands but we are studying this method further. Second, it illustrates that hypoproteinemia can develop rapidly following serious operations even though the patient is in apparently good nutritional balance before operation.

Disturbances in wound healing. Experimental work on wounds has demonstrated that the principal essential for rapid healing is multiplication and growth of fibroblasts. Harvey and Howe have divided the period of wound healing into three phases: (1) the lag period, (2) the period of fibroplasia when the velocity of healing is changing most rapidly, and (3) the phase of approaching maximum immediate strength. Clarke, in 1919, in studying the effect of diet on the healing of wounds determined that a high protein diet shortened the lag phase and produced a decrease in the time necessary for initiation of the growth of fibroblasts. He believed that proteins were necessary for proper wound healing. Harvey and his co-workers have also emphasized the importance of proteins but they believe that the lag phase is not affected. They have found an increase in the velocity of growth of fibroblasts with a high protein diet but no change in the duration of the lag phase or in the maximum strength of the healing wound, although this last phase is reached sooner. Thompson and his associates first demonstrated that an artificially induced hypoproteinemic state in dogs interfered with the healing of visceral and surface wounds in over 70 per cent of the animals. In these cases either disruption of the wound or delayed healing occurred, but when the serum proteins were restored to normal by the administration of lyophilized plasma, wound healing rapidly occurred (29).

This interference with wound healing associated with hypoproteinemia has been observed frequently by us. In 1 case previously reported (4) complete disruption of the abdominal incision occurred and secondary suture failed to cause healing. The serum proteins of this patient were consistently below 3.5 grams per 100 cubic centimeters and all efforts to raise the level were fruitless. Needless to say, death quickly ensued. In Case 2, disruption of the wound also occurred and though an appendiceal abscess was present, the wound was not grossly infected, and presented the edematous appearance common to these patients. In the cases observed by us, the wounds were clean, edematous, glistening, pale, and anemic in appearance. These findings have been reported in hypoproteinemic dogs by Thompson. The question of whether edema *per se* will cause delay or absence of wound healing is to be seriously considered. While the evidence of the importance of proteins in accelerating fibroblastic proliferation is conclusive, it is well known that incisions into edematous tissues usually heal poorly. Thompson, in the studies referred to, found that edema of the wound edges persisted for varying periods after the serum proteins had been restored to normal and this did not inhibit repair of the wounds. It is probable that both factors; i.e., specific absence of protein

(or possibly of certain amino acids) and the resulting tissue edema, operate to delay wound healing in these cases. It would be interesting to produce edema by excess salt administration and maintain the serum proteins at a normal level and study the effect on experimental wounds.

Case report. A. R., No. 78483, a white male, 16 years of age, was operated upon for an appendiceal abscess on August 19, 1939. On the tenth day after operation signs of a mechanical intestinal obstruction developed and on August 31, 1939, the abdomen was opened through a suprapubic incision. A strangulating, adhesive band obstruction was found and released. A small perforation of the ileum was closed by a pursestring suture and the wound closed without drainage. On September 9, extensive edema of the thoracic and abdominal wall and hydrothorax was noted. The serum proteins were 5.5 grams per cent and the albumin was reduced to 3 grams per cent. Marked distension occurred but was controlled with a Miller-Abbott tube. On September 13, the second incision disrupted but no evisceration occurred. The serum proteins were unchanged from the level of the previous examination. Hydrothorax, pulmonary edema, and edema of the face and hands soon followed. Multiple transfusions were given and a high protein diet administered through the indwelling tube. On September 18 the edema had largely disappeared and by October 1 it had completely disappeared. Healing of both wounds had remained practically stationary during this period. On October 2 the serum proteins had risen to 8.6 grams per cent and the albumin fraction was 4.8 grams per 100 cubic centimeters. After this healing became much more rapid and the remainder of the course was uneventful.

In this case again, the warning sign of peripheral edema antedated wound disruption but was overlooked, no transfusion or protein therapy being instituted until after dehiscence occurred. We cannot stress too strongly the importance of the early signs of hypoproteinemia which, although probably innocuous in themselves, should direct our attention to the underlying nutritional state before more serious sequelæ occur.

TREATMENT

The treatment of hypoproteinemia should be prophylactic. All patients about to undergo serious operative procedures should be carefully studied for disturbances in their nutritional status, with particular reference to serum proteins, vitamins, and fluids. If actual depletion of serum proteins is discovered, the operation should, if possible, be postponed until the normal concentration is restored. It is much easier to do this before than after operation and frequently a high protein diet will suffice. If the patient is unable to retain or absorb the necessary food elements when administered by mouth, other methods which will be described subsequently must be instituted. Unfortunately, however, the presence of severe nutritional disturbances as manifested by hypoproteinemia is not usually discovered until complications ensuing in the postoperative period indicate that the protein metabolism is disturbed.

The restoration of diminished serum protein to normal is not always a simple task and is dependent on two factors: (1) whether there is damage to the regenerating mechanism; and (2) whether the abnormal loss of protein can be stopped. As a rule, the second factor can be controlled without much difficulty or sufficient protein can be administered to counteract this loss. The first factor, however, is much more significant. If the ability of the organism to regenerate the proteins of the serum is impaired or destroyed, no amount of protein which can be administered will do more than act as a temporary substitute for the proteins already lost. As yet, no method whereby this mechanism can be sustained or repaired is known, and, as a matter of fact, the nature of the mechanism is still in doubt. There is some evidence that the liver or possibly the cells of the entire reticulo-endothelial system are the site of the formation of serum proteins and as is well known, these cells are frequently injured or their function impaired. Among other factors, anesthesia, sepsis, and anoxemia may adversely affect these structures and interfere with their protein regenerating function. It is in these patients that the problem of sustaining the level of serum proteins assumes such magnitude. We have seen such cases, and have seen many case reports in the literature, wherein the serum proteins were diminished and could not be replenished despite the administration of large amounts of protein. Recently a patient was observed who was suffering from acute yellow atrophy of the liver and in whom a severe hypoprotein-

emia developed. It was impossible to raise his protein concentration appreciably despite the administration of large amounts of protein by mouth and repeated massive serum transfusions. In this case the mechanism for regenerating serum proteins was seriously inhibited. Other patients exhibit this same phenomena without obvious liver disease and they present the same great problem in therapy.

The administration of protein by mouth either as whole proteins or amino acids is obviously of no value as these cannot be utilized and synthesized to form serum protein. By supplying the necessary protein in a utilizable form, serum transfusions are a temporary expedient but they may be sufficient to carry the patient until any injury to the serum-regenerating cells may have time to heal. Occasionally, this is inadequate and the patient eventually dies of this deficiency. Melnick and Cowgill have stressed the point that until the nature of the mechanism which controls the regeneration of serum proteins is better understood, the approach to therapy can be only symptomatic and haphazard.

It is fortunate that many, if not most, of the surgical patients who develop hypoproteinemia exhibit no serious defect in the regeneration of serum proteins. The deficiency is usually amenable to treatment without much difficulty and consequently we feel that the impairment in the mechanism of protein regeneration is slight. It is debatable whether administration of proteins acts as a stimulant to serum protein regeneration, and Weech (30, 31, 32, 34) was unable to determine any correlation between the administration of proteins and the rate of regeneration. There is, however, some experimental work which indicates that malnutrition may affect the liver and impair its ability to synthesize serum proteins. Probably the restoration of the nutritional state to normal remedies this disability; at any rate it is an established fact that very frequently the proper administration of protein does replenish the serum proteins and overcomes hypoproteinemia with its concomitant manifestations. In this connection the administration of large amounts of glucose may be of value because of the beneficial effect on the liver and because of its caloric value.

Proteins may be given by mouth, by rectum or parenterally. Unquestionably, the method of choice when feasible is the oral route. The absorption of the split products of protein digestion normally occurs in the small intestine and in the ordinary course of events the material for building serum proteins is obtained in this way. In the pre-operative period little difficulty is encountered in administering sufficient proteins by mouth. For some time we have been preparing our surgical patients by feeding a diet containing 25 per cent of proteins for several days or a week before operation. Occasionally patients are unable to take or retain food by mouth because of their surgical condition. The presence of peptic ulcers, pyloric obstructions, intestinal fistulas, and other similar conditions may contra-indicate oral feedings. In these cases we have frequently been able to institute feedings through an indwelling tube. Recently Stengel and Ravdin have reported an excellent method of administering protein through a Miller-Abbott tube by using an intermittent pressure pump. They have had considerable success with a peptone hydrolysate mixture. We have used whole protein in our patients with good results. In the post-operative period oral feedings are usually contra-indicated and at this time the device of Stengel and Ravdin is of immeasureable value. Following gastric resection or gastro-enterostomy the tube is drawn through the stoma and feeding can be started almost immediately. We have had no experience with rectal feedings of proteins but the work of Ravdin and of Rhoads and his co-workers seems to indicate that some absorption of protein split products does take place in the colon and this route may be utilized if necessary.

The parenteral administration of proteins is invariably by the intravenous route. Whole blood or plasma are the two agents most commonly employed. The use of whole blood is of particular value when hypoproteinemia is associated with anemia. It is important to give multiple, large, and frequent transfusions if a definite rise in the serum proteins is to be

obtained and maintained. We have noted elevations of 0.2 to 0.4 grams per 100 cubic centimeters immediately following transfusion of 500 to 1000 cubic centimeters of blood but within 24 hours this may be lost if further transfusions are not administered. The use of plasma or serum presents several advantages over whole blood. In the absence of anemia, it does not overload the circulation with red blood cells which are not needed. Secondly, it may be stored indefinitely without deterioration, in marked contrast to whole blood; and thirdly, if pooled serum is used, it need not be of the same type as the patient's blood. Plasma or serum transfusions afford a method of administering concentrated serum protein quickly and easily, and with a minimum of reaction. Our experiences have been very satisfactory but the admonitions in regard to the use of whole blood must be carried out. Frequent and large infusions must be given. We have administered 1000 cubic centimeters of plasma several times and have noted no untoward reactions.

The use of desiccated or lyophilized plasma described by Flosdorf and Mudd has been suggested but we have had no experience with this preparation. Ravdin, Stengel, and Prushankin report severe reactions following the use of lyophilized plasma. Recently Elman and Weiner reported their experiences with the administration of amino acids derived from the hydrolysis of casein with the addition of tryptophan and cystin. They have used this mixture in many cases without any demonstrable deleterious effects and in many cases were able to elevate the serum proteins appreciably. In many cases, however, despite apparent clinical improvement, no rise in the serum proteins was observed. In these cases, doubtlessly, the temporary clinical improvement was attributable to the transient increase in the osmotic pressure of the blood but apparently no regeneration of proteins occurred in the patient. Whereas amino acids when given intravenously must be synthesized into serum proteins within the organism, plasma is immediately available for use and hence serves as a more efficient substitute for the lost proteins. However, when there is no striking interference with the regenerative function of the patient, it would seem that amino-acids should be of great value. At any rate this method of "intravenous alimentation" has great possibilities in the treatment of temporary diminutions in the serum protein level, and is certainly worthy of further study. The importance of the proper selection of amino-acids cannot be overestimated, however. It has been demonstrated conclusively that certain amino-acids are indispensable for serum protein regeneration. Both cystin and tyrosine must be present, either in the diet or in the parenteral medication, to provide the necessary elements for the formation of the protein of the serum (17). While phenylalanine and methionine are indispensable for tissue growth they play a minor rôle in the rebuilding of the serum protein. This has been recognized by Elman and his associates in planning the character of the intravenous solutions they employed.

It would seem from the foregoing that the therapy of hypoproteinemia rests on an insecure foundation. Fortunately, the majority of cases are either improved or cured by the substitution of serum proteins or by the administration of the essential elements which constitute these proteins. In the cases resistant to this therapy, attention must be given to the liver. There is ample evidence that a high protein intake in addition to carbohydrates is essential to protect the liver from damage by anesthetic agents or other noxious substances. This consideration should guide our pre-operative as well as postoperative care and may prevent hypoproteinemia from developing. We feel that the use of large amounts of intravenous glucose in a 10 per cent solution in distilled water plus a high protein diet by mouth or through an indwelling tube is the best means of preparing the liver for the shock of surgery, or treating it when it has already been damaged. In addition, the free use of plasma transfusions has, in our hands, been the surest and swiftest method of causing at least temporary rises in the serum proteins in hypoproteinemic patients.

SUMMARY AND CONCLUSIONS

1. Evidence is presented which suggests that hypoproteinemia is caused by impair-

ment of the mechanism or organ which is responsible for the production of serum proteins. The "loss and lack" theory does not explain the variations in the metabolism of serum proteins.

2. There is some evidence to indicate that the liver is the site of regeneration of serum proteins.

3. Edema is a result of hypoproteinemia. This edema is attributable to alterations in the mechanics of fluid distribution between the vascular channels and the extravascular spaces which are caused by a decrease in the colloidal osmotic pressure of the blood induced by a deficiency of the serum albumin. However, many other factors may influence this edema. Among these are the following: tissue elasticity, water balance, and the character and distribution of the electrolytes of the body fluids.

4. The clinical manifestations of hypoproteinemia are varied but almost all can be explained on the basis of disturbances in fluid distribution. The principal manifestations are: peripheral edema, pulmonary edema, disturbances in gastro-intestinal motility and disturbances in wound healing.

5. Treatment is not always satisfactory inasmuch as the exact mechanism responsible for the production of serum proteins is unknown. Since the liver plays a definite and important rôle, therapy should be directed toward protecting and sustaining this organ. A high protein and carbohydrate intake is essential.

6. Substitution therapy in the form of whole blood or plasma transfusions, parenteral administration of amino acids, or orojejunal feeding of amino acids, has met with some success. In our experience, the administration of massive transfusions of plasma has provoked the greatest and most sustained rise in the serum proteins.

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AN EXPERIMENTAL STUDY OF URETERO-INTESTINAL IMPLANTATION

IV. The Significance of Ureterovesical Reimplantation in the Dog

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CLINICAL experience and experimentation on animals have yielded abundant proof of the danger which attends one-stage bilateral uretero-intestinal anastomosis. Implanting the ureter into the large intestine initiates a sequence of pathological changes which commonly result in obstruction of the upper urinary tract and ascending infection. Since both kidneys are affected simultaneously in the one-stage operation, these complications are likely to terminate fatally. If one ureter is implanted, however, and a period of a few weeks is allowed to elapse before the second ureter is transplanted, the kidney on the side of the first operation will have recovered sufficiently from the brunt of the early damage to enhance the possibilities of success.

These facts make it clear that the acid test of any method of uretero-intestinal anastomosis is the result attending the one-stage operation. When a means is found of assuring a uniformly successful outcome following this procedure the hazards of obstruction and ascending infection will have been surmounted and the merit of the operation firmly established. While not justified in human cases, attempts to perfect the one-stage bilateral transplant offer a fertile field for investigation in animals.

It was with a view to appraising the part played by the highly infected nature of the field into which the end of the ureter is implanted in uretero-intestinal anastomosis that a one-stage bilateral ureteroneocystostomy was carried out in 6 dogs. The wall of the bladder is sufficiently similar to that of the large intestine to make it possible to perform a submucosal ureterovesical reimplantation identical in all respects to a uretero-intestinal anastomosis, the only variable factor being the contamination from the rectosigmoid in the latter procedure.

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EXPERIMENTS

The operations were performed in the following manner: The dog was anesthetized with ether and the peritoneal cavity was entered through a low midline incision. Following exploration of the kidneys, the bladder and lower portion of the ureters were exposed by packing the small intestines into the upper part of the abdomen. The pelvic peritoneum was incised longitudinally at the base of the mesosigmoid and the ureters were freed throughout their lower third.

The left ureter was reimplanted first. It was clamped and divided in its juxtavesical extent and the distal stump was tied off. A site for reimplantation was selected along the lateral wall of the bladder and the area marked with two stay sutures. The detrusor muscle was incised for a distance of 1.5 centimeters between these markers, the edges of the incised muscle being dissected back to expose a diamond-shaped area of submucosa (Fig. 1). Three sutures of 0000 chromic catgut were then placed from the adventitia of the ureter to the submucosa of the bladder so as to form a triangle at the distal end of the exposed submucosa. A small perforation through the submucosa and mucosa in the center of the triangle was made with the point of a No. 11 blade. After a specimen of urine was aspirated through the opening, the proximal end of the divided ureter was introduced.

As a part of the study of the destiny of the end of the ureter[1] the end was left long in some instances, short in others. The ureter was anchored by tying the 3 primary sutures (Fig. 2A), and the anastomosis was reinforced by uniting the edges of the detrusor muscle over the distal part of the incision with a few interrupted sutures.

The right ureter was reimplanted in a similar manner (Fig. 2B) and the abdominal wound was closed without drainage. No attempt was made to extraperitonealize the anastomoses.

The specimen of urine obtained from the bladder in one instance contained pus and gram-positive bacteria (confirmed by culture); the others gave no evidence of infection.

RESULTS OF EXPERIMENTS

The animals suffered no apparent ill effects from the operation but continued in excellent health until they were killed—2 at the end of 1 week and the others at 1 month, 2 months, 10 weeks, and 6 months, respectively. The results of the necropsies are summarized in Table I (Fig. 3).

[1]An experimental study of uretero-intestinal implantation. V. The destiny of the implanted ureter. (In press.)

Fig. 1. Ureterovesical reimplantation in the dog. Both ureters are freed throughout their lower third. The left has been divided and its site of reimplantation prepared by an incision down to the submucosa.

In only 2 animals was there evidence of obstruction of the upper urinary tract, a mild bilateral hydro-ureter and hydronephrosis being observed in both dogs killed at 1 week (Fig. 3, A and B). A blood non-protein

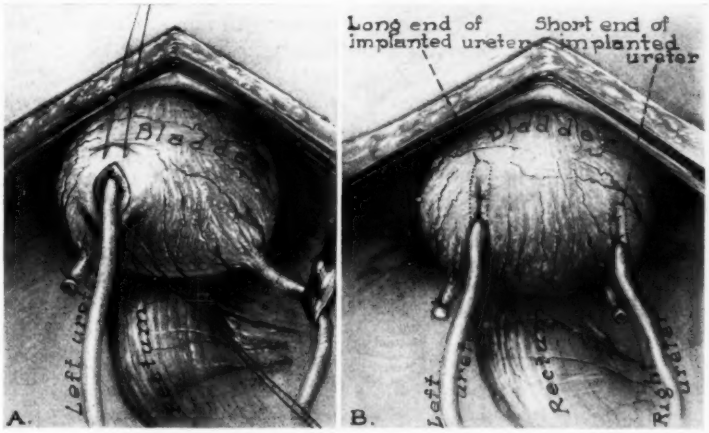

Fig. 2. Ureterovesical reimplantation in the dog. A, The end of the left ureter has been inserted through an opening into the cavity of the bladder. It is anchored in place by three sutures joining the submucosa of the bladder to the adventitia of the ureter. B. Both ureters have been reimplanted. The anastomosis is reinforced by sutures uniting the detrusor over the submucosal course of the ureter.

TABLE I.—SERIES OF ONE-STAGE BILATERAL URETEROVESICAL REIMPLANTATIONS IN THE DOG (SEE FIG. 3)

No.		Technique: bilateral submucosal reimplantation	Culture of urine from bladder*	Sacrificed at	Ascending infection	Obstruction upper tract	Blood NPN at necropsy mgm.	Length of end of ureter	Peritonitis	Wound infection
Exp.	Dog									
A	30	Right: Long end Left: Short end	No growth	1 week	Mild Mild	Mild Mild	35	1.2 cm. .6 cm.	0	0
B	33	Right: Long end Left: Short end	Gram-positive rods	1 week	Mild Mild	Mild Mild	45	3 cm. 1 cm.	0	0
C	496	Right: Long end Left: Short end	No growth	1 month	0 0	0 0	28	1 cm. 0	0	Superficial
D	497	Right: Short end Left: Long end	No growth	2 months	Mild 0	0 0	31	0 0	0	0
E	498	Right: Long end Left: Short end	No growth	10 weeks	Mild 0	0 0	25	0 0	0	0
F	493	Right: Short end Left: Long end	No growth	6 months	0 0	0 0	28	0 6 mm.	0	0

*Obtained at operation.

nitrogen at the upper limit of normal in one and a slightly elevated reading in the other gave evidence of mild impairment in renal function. Since these changes were not present in the animals killed later it is reasonable to conclude that they resulted from an early temporary period of partial obstruction induced by operative trauma.

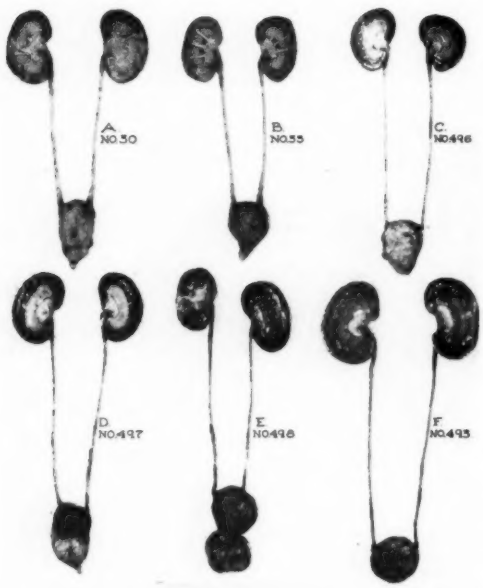

Fig. 3. Changes in the upper urinary tract following bilateral ureterovesical reimplantation (see Table I).

Examination showed no hyperemia or other gross evidence of inflammation of the ureters or kidneys although, upon microscopic section, a mild bilateral ureteritis and pyelonephritis were observed in the dogs killed at 1 week, and a similar unilateral involvement was noted in those sacrificed at 2 months and 10 weeks. This reaction was manifested by an infiltration with leucocytes of parts of the submucosa and adjacent areas of the renal pelvis and ureter (Fig. 4). The redundant intravesical end of the ureter sometimes demonstrated a more violent reaction shortly after operation. Although the mucosa, submucosa, and muscularis were almost free from infection, the adventitia showed a dense infiltration of polymorphonuclear leucocytes surrounded by an inflammatory débris (Fig. 5).

Peritonitis did not occur, nor was there any serious wound infection. A superficial suppuration of the skin incision developed in one animal.

ANALYSIS OF STUDY

It is interesting to note that only the mildest and most transient forms of ascending infection and obstruction occurred following this series of ureterovesical reimplantations. Such findings are in dramatic contrast to the frequency and severity of these complications after uretero-intestinal anastomosis.[1] For example, in a typical control series of 6 dogs subjected to bilateral uretero-intestinal anas-

[1]An experimental study of uretero-intestinal implantation. VI. The relation of ascending infection to ureteral obstruction. (In press.)

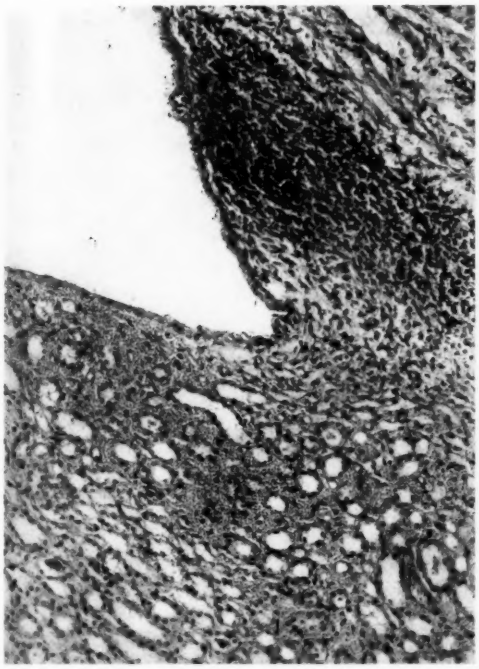

Fig. 4. Typical form of ascending infection occasionally observed following ureterovesical reimplantation—mild pyelonephritis is evidenced by a leucocytic infiltration limited to a small area immediately surrounding the renal pelvis. Dog killed after 1 week. (Right kidney, Dog A, Fig. 3, and Table I.)

Fig. 5. Acute inflammatory reaction surrounding redundant stump of ureter sometimes observed shortly after ureterovesical reimplantation. The mucosa, submucosa, and muscularis are scarcely involved, but the adventitia is encased in a zone of inflammatory débris. Note the dark clumps of bacteria near the periphery. Dog killed at 1 week. (Left ureter, Dog A, Fig. 3, and Table I.)

tomosis, instead of any recession of the early obstructive changes, advanced degrees of late hydronephrosis, hydro-ureter, and severe renal infection resulted (Fig. 6). These differences were likewise apparent in another control series in which one ureter was reimplanted into the bladder and the other into the rectosigmoid. With an almost uncanny regularity ascending infection and obstruction attended the intestinal transplant while the side reimplanted into the bladder escaped with only the mildest changes (Fig. 7). In the two control series the 18 implants into the large intestine progressed to moderate and advanced degrees of obstruction and infection in almost every instance, whereas the 6 reimplantations to the bladder produced only a mild ascending infection and obstruction in one animal (at 6 days), and a mild hydroureter in another (at 6 months). The remainder of the upper tracts were normal following ureterovesical reimplantation except for a hematogenous renal infection observed in the animal killed at 9 weeks.

These results permit only one conclusion, that the serious degrees of ascending infection and obstruction are directly attributable to the degree of contamination of the field into which the end of the ureter is introduced.

A feature of some encouragement in the ureterovesical reimplantations is that uniformly good results were attained despite the occurrence of mild degrees of infection. This finding suggests two important questions as concerns the final conquest of ascending infection and obstruction: First, just what degree of infection will be tolerated in the field of implantation without compromising a satisfactory outcome, and, second, is it pos-

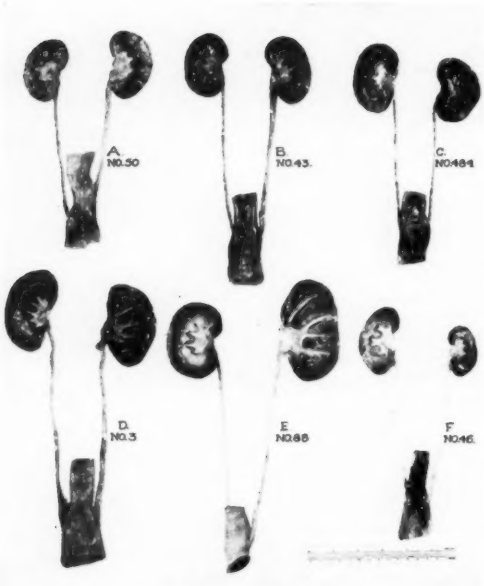

Fig. 6. Changes in the upper urinary tract following bilateral uretero-intestinal implantation.

No.	Side	Time following operation	Ascending infection	Obstruction
A 50	Right	4 days	Severe	Mild
	Left		Moderate	Mild
B 43	Right	5 days	Moderate	Mild
	Left		Moderate	Mild
C 484	Right	1 week	Moderate	Mild
	Left		Moderate	Mild
D 3	Right	1 month	Moderate	Severe
	Left		Moderate	Severe
E 88	Right	1 month	Moderate	Moderate
	Left		Moderate	Severe
F 46	Right	4 months	Severe	Severe
	Left		Severe	Moderate

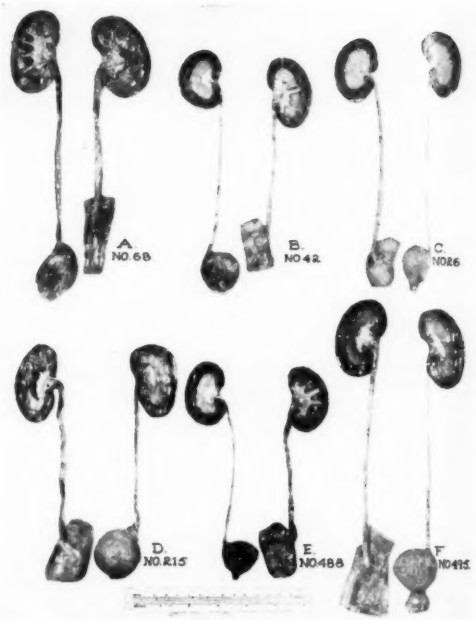

Fig. 7. Changes in the upper urinary tract following ureterovesical reimplantation on one side, and uretero-intestinal anastomosis on the other.

No.	Site of implant	Time following operation	Ascending infection	Obstruction
A 68	Right: Bladder	6 days	Mild	Mild
	Left: Intestine		Severe	Moderate
B 42	Right: Bladder	1 month	o	o
	Left: Intestine		Mild	Moderate
C 26	Right: Intestine	1 month	Mild	Mild
	Left: Bladder		o	o
D 215	Right: Intestine	6 weeks	Mild	Moderate
	Left: Bladder		o	o
E 488	Right: Bladder	9 weeks	Focal Hematogenous	o
	Left: Intestine		Severe	Severe
F 495	Right: Intestine	6 months	Moderate	Moderate
	Left: Bladder		o	o

sible to reduce the degree of infection in the large intestine sufficiently to meet this criterion, whatever it may be, during the post-operative period of healing? Following epithelization of the mucous surfaces of the uretero-intestinal junction and healing by primary union of the other tissues involved in the anastomosis, the period of danger is passed. Conditions then correspond to the normal arrangement found in some species of animals, an arrangement entirely compatible with a normal upper urinary tract.[1]

It would be possible to gain some idea of the amount of infection which is compatible

[1]Surg., Gynec. & Obst., 1939, 69: 713–716.

with satisfactory healing of a ureteral implant by performing a series of reimplantations following graduated contamination of the bladder. It is of more practical interest, however, to investigate the means and effect of reducing the bacteria in the large intestine at the time of uretero-intestinal anastomosis.

Conservative measures, such as a non-residue diet, adequate catharsis, multiple enemas, and the administration of urinary antiseptics have improved the results of the operation, yet they fall short of yielding the final solution to the problem.

The futility of forming an artificial bladder was early demonstrated. While tremendously increasing the operative risk, both the complete and partial exclusion of a part of the large intestine failed in their fundamental purpose, that of providing a sterile reservoir for urine.[1] It was found impossible to sterilize these stagnant urinary pockets, even by frequent irrigation with antiseptic solutions.

In view of these experiences the value of a temporary colostomy in diverting the fecal stream is questionable. Nevertheless, the problem is one of such fundamental importance that it is our purpose to determine to what extent, if any, a temporary colostomy supplemented by irrigations of the distal loop will improve the results of one-stage bilateral uretero-intestinal anastomosis in the dog.

From a clinical standpoint the results would have to be indisputable in order to justify the incorporation of another surgical procedure, if not another stage, to the accomplishment of a uretero-intestinal anastomosis. On the other hand, no effort is too great which would effectively reduce the morbidity and high mortality now exacted by ascending infection and obstruction.

[1]A critical study of the different principles of surgery which have been used in uretero-intestinal implantation. Tr. Am. Ass. Genito-Urin. Surg., 1936, pages 15–156; and Internat. Abstr. Surg., 1937, 313–363.

We are intrigued by still another possibility, less radical than colostomy, but more revolutionary in character. We refer to the possibility of cleansing the mucous surfaces by continuous irrigation of the rectosigmoid. Despite the general policy of delaying lavage until healing is complete there should be no danger of peritonitis, even in the early postoperative days, if the intestine is not overdistended. A continuous current of fluid would remove urine and fecal matter (substances which provide such excellent culture media for bacteria) from around the end of the ureter. This mechanical cleansing should prove more important than any antiseptic quality of the fluid used. If an antiseptic were to be employed for this purpose, poisonous substances should be avoided because of the absorptive activity of the intestine.

SUMMARY AND CONCLUSIONS

A one-stage ureterovesical reimplantation was performed in 6 dogs by a technique similar to submucosal uretero-intestinal anastomosis. The only variable factor was the absence of the contaminated field into which the end of the ureter is introduced in the latter operation.

Upon comparing the almost entire absence of ascending infection and obstruction of the upper urinary tract after ureterovesical reimplantations with their common occurrence in uretero-intestinal transplants, one is forced to conclude that serious degrees of these dangerous complications are directly attributable to the overwhelming infection which is present in the large intestine.

It is apparent, therefore, that a line of investigation searching out every possible means of reducing or eliminating infection in the rectosigmoid during the period of healing constitutes one of the key problems to the final perfection of uretero-intestinal anastomosis.

THE GENESIS OF PEPTIC ULCER IN DOGS FOLLOWING LIGATION OF THE COMMON BILE DUCTS

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SINCE Cruveilhier first described peptic ulcer about a century ago it has been rather generally agreed that the two factors necessary to the production and maintenance of ulcers of the gastric and duodenal mucosa are injury and devitalization of the gastric or duodenal epithelium followed by digestion and continued irritation of the injured area by gastric ferments and acid. Ivy lists mechanical damage, heat, drugs, toxins, peptones, serums, section of the vagus and splanchnic nerves, embolism, thrombosis, anemia, feeding and intravenous injection of specific and nonspecific bacteria, central nervous system lesions, removal of the suprarenal and parathyroid glands as agencies, which will cause petechial hemorrhages, superficial hemorrhagic erosion, and acute ulceration. Shore has included localized hemorrhage in the gastric mucosa as a type of injury which may be followed by gastric digestion and ulcer formation. Finally Lipschutz has suggested that the initial injury to the gastric or duodenal mucosa may be anaphylactic in origin.

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Fig. 1. Multiple, small, spontaneous hemorrhages in the gastric and duodenal mucosa 5 weeks after ligation of the common bile duct. Notice that only one hemorrhagic area near the lower margin here is ulcerating.

Following the initial lesion there are far fewer factors apparently at work, most observers agreeing with Bolton (6) that chronic ulcer originates from the acute lesion, being maintained and healing prevented by the digestive and irritating action of gastric acid. Moynihan, however, believed that ulcers would exist very often in a diminished acid medium and that a high gastric acidity was not essential to ulcer maintenance.

In the dog, spontaneous gastric or duodenal ulcers occur but are not common. Turck, in a series of autopsies on 189 healthy and 82 diseased dogs, found no ulcers in the stomach or duodenum. Mann (12) found no lesions of the gastric mucosa in 200 autopsies on normal cats and dogs. Ivy found only 1 acute gastric ulcer in a series of 900 dogs used for laboratory experimentation. Experimental gastric and duodenal ulcers, however, have been reported in dogs by many investigators and due to many causes. Bolton (5) was able to delay the healing of experimental acute ulcers by producing partial pyloric stenosis. Turck produced perforating ulcers of the stomach and duodenum by feeding Bacillus coli, and Rosenow could produce them by the intravenous injection of alleged specific streptococci. Durante could produce chronic ulcers by ligating and cutting the splanchnic nerves. Ivy produced ulcers by aseptic embolism with lead chromate but was unsuccessful when finely divided charcoal was used by the same technique. Mann and Williamson (13) were able to produce ulcers in experimental animals by elimination of the secretions normally poured into the gastro-intestinal tract beyond the pylorus. They felt that these ulcers were chemical in character. Following the suggestion of Still and Carlson that gastric ulcers followed a change of gastric motility associated with liver disease, Bollman, Stalker and

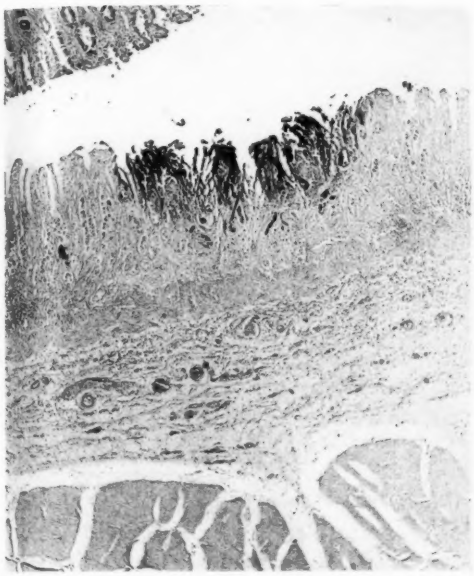

Fig. 2. Section of one of the small mucosal hemorrhages in the stomach. ×97.

Fig. 3. Section of the one ulcer in Figure 1 showing digestion of the hemorrhagic portion of mucosa. ×97.

Mann (4) gave cinchophen to dogs in large doses and while most of the animals failed to show demonstrable liver lesions, many did develop areas of ulceration in the gastric or duodenal mucosa. Bollman and Mann (3) produced gastric or duodenal ulcers in about 60 per cent of a group of dogs by ligating the common bile ducts. These, like the Mann-Williamson ulcers, were thought to be due to the absence of alkaline bile with which to neutralize gastric acid.

While the specific etiology of gastric and duodenal ulcers in canines remains as uncertain as it does in human beings there seems to be no question that one of the direct associates of such ulcers is extraduodenal diversion of bile. Kapsinow and Harvey, using a cholecystonephrostomy, produced ulcers in 17 of 43 animals. Berg and Jobling found ulcers in 13 of 23 cases in which a Rous type of fistula was used. Berg felt that the general condition and cachexia of the animals had a definite relationship to ulcer formation, but Andrews and Bissell did not find any such direct association between cachexia and ulcer formation. They further concluded that the initial formation of these ulcers was dependent upon some other factor than acid. In addition, the absence of the neutralizing effects of bile has been shown by Goldman to have little or no effect on the

Fig. 4. Sections showing digested and undigested mucosal hemorrhage side by side. ×14.

Fig. 5. Two large chronic penetrating peptic ulcers.

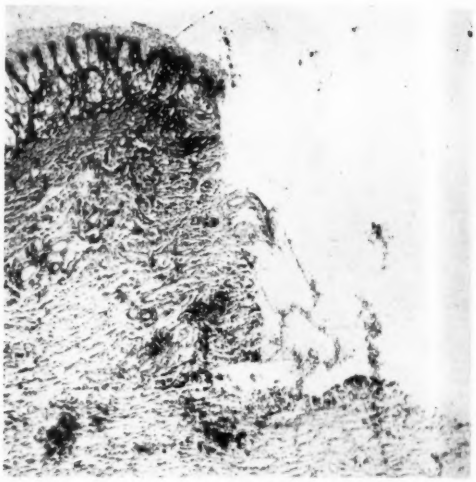

Fig. 6. Section of upper ulcer in Figure 5 showing perforation through the muscularis mucosa. ×28.

formation of ulcers of the gastro-intestinal tract and while cinchophen will produce ulcers no definite proof has been offered that these lesions are due to liver damage.

In a recent series of 20 dogs, which were being studied for prothrombin changes following ligation of the common ducts, 11 showed gastric or duodenal ulcers at autopsy after icterus of 3 weeks or more. These animals had been fed an especially prepared diet of sucrose, cracker meal, beef extract, salt mixture, Fuller's earth, and adequate amounts of all the vitamins excepting K and E. They followed the usual course of dogs with obstructive jaundice as described by us (7) and others.

There was no observable variation in the nutrition or appetite of individuals with and without ulcer, but at autopsy changes were seen in the gastric mucosa which suggest the bleeding dyscrasia in obstructive jaundice as a background for breaking the continuity of the gastric or duodenal mucosa rather than lack of neutralization of gastric acid or a deficiency state because of acholia and incomplete gastro-intestinal absorption.

Of the 11 animals developing ulcers, 9 had gastric lesions, and 2 had ulcers in the duodenum. Of the gastric series only 1 was solitary and the others were either in pairs or multiple. Of the duodenal ulcers, 1 showed two ulcerations while the other had a single ulcer which had perforated into the gall bladder forming a spontaneous cholecystoduodenostomy.

The genesis of these ulcers was observed through successive changes from early mucosal hemorrhage to complete ulceration and digestion of the mucosa. This series we feel illustrates the cytological steps in ulcer formation and establishes this particular type of gastric and duodenal ulcer as a part of the hemorrhagic diathesis of obstructive jaundice.

State 1. Dogs in which the common bile ducts have been ligated begin to develop abnormal bleeding tendencies 3 to 4 weeks after operation. Hemorrhages may occur spontaneously, after injury has occurred, or following surgery.

In the first instance bleeding may occur from any epithelial surface including the mucosa of the gastro-intestinal tract. These hemorrhages are small to petechial, are of slow oozing character, and usually stop spontaneously with repair of the epithelium (Figs. 1 and 2). In the stomach and duodenum the digestive juices attack the part of the mucosa in which the hemorrhage has occurred and, in a small percentage of these areas, the epithelium in its entire depth down to the muscularis mucosæ is destroyed. There is at this time little or no inflammatory reaction in these areas (Figs. 3 and 4).

Stage 2. Once the gastric mucosa is broken such ulceration follows the same course as any other type of gastric or duodenal ulcer with gradual infection of the ulcer crater and cicatrization of the bed. Epithelization is prevented by the constant action of digestive juices, and such ulcers go on to a chronic state with penetration and occasional perforation (Figs. 5 and 6).

SUMMARY AND CONCLUSIONS

In a series of 20 dogs, following ligation of the common bile ducts, 9 developed gastric and 2 duodenal ulcers 3 to 8 weeks after operation.

Such ulcers were started by physiological digestion of spontaneous hemorrhages in the mucosa of the stomach and duodenum which occurred as part of the hemorrhagic diathesis of obstructive jaundice.

Once such breaks in the continuity of the mucosa were established, these ulcers followed the same clinical course as others of similar size in the same locations.

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THE CLINICAL VALUE OF THE SERUM AMYLASE TEST

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THE significance of the serum amylase determination as a valuable and reliable diagnostic aid has long been the subject of considerable clinical uncertainty. Tests of biliary and kidney function have been so profitable that a similar usefulness seemed possible in the diagnosis of deceptive pancreatic disease. From a review of the literature regarding amylase there appears to exist noteworthy disagreement and lack of experimental uniformity which might readily nurture seeds of clinical caution and doubt. However, recent investigators have rather successfully challenged some of these discrepancies, and qualified certain other discordant results as being more apparent than real. Technical variation has inevitably been responsible for some dissension among observers; yet, if serum amylase values are regarded only with comparative and *not* quantitative accuracy their reliability assumes a new importance and may well satisfy a most helpful diagnostic rôle. A lack of ultimate quantitative precision should not impugn the clinical value of the serum amylase test. It is of more genuine diagnostic importance to determine the deviation from the normal amylase limit than to ponder the significance of some isolated unit of activity.

Conflicting results and disagreement among competent authors have been generally attributed to a difference in the methods of investigation and to the confusing arbitrary units and intangible values used to express amylase activity. Fundamentally the subject is a most complicated one and fraught with many perplexing physicochemical problems, yet its clinical application is simple and readily carried out. The basic need for a proper standardization of optimum hydrogen ion concentration, electrolyte content, temperature, amount of substrate, and reaction time has been fully realized by Davison (1925), Elman and McCaughan (1927), Muhlfeld (1928), Meyers and Reid (1933), Schmidt, Greengard and Ivy (1934), Somogyi (1938), and others. Although a final correlation and evaluation of this quantitative chemical data regarding amylase cannot be made at present, a plan of procedure has been outlined and further investigation should considerably enhance the development of the kinetics of enzyme chemistry.

In 1833 Payen and Persoz first precipitated a starch-splitting product from malt which they named diastase. Magendie (1846) noted the presence of a ferment in the blood capable of changing starch to sugar. By injecting starch intravenously he found that after 10 minutes the blood no longer gave a starch-iodine reaction, but that the content of blood sugar had increased considerably. Claude Bernard, préparateur to the master, Magendie, at the Collège de France, was an eminent contributor to the study of sugar metabolism and the rôle of pancreatic juice in the process of digestion. In 1849 his studies led him to believe that the action of pancreatic juice upon starch was not a special property of that organ alone, but that saliva and blood serum also had a similar amylolytic activity. Foster (1866–67) found amylase[1] widely distributed in the animal body and, by noting the time required for the conversion of a given quantity of starch, roughly determined the amount of ferment present. He observed that the blood and urine amylase of six diabetic patients in no way exceeded that found normally.

Carlson and Luckhardt (1908–09), in reviewing the more important contributions to the subject, pointed out that Bainbridge and Beddard (1907) found no disappearance of blood amylase following pancreatectomy in cats. Schlesinger (1908), on the contrary, extirpated the pancreas in two dogs and one cat and reported the complete disappearance

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[1] The terms *amylase* and *diastase* are used synonymously by most authors. We prefer the more descriptive term amylase and in this paper will use it exclusively.

of the enzyme. Wohlgemuth (1908), Kaufmann (1894), Lepine and Barral (1891), and others observed only a partial diminution of blood amylase following pancreatectomy. Carlson and Luckhardt, using (1) the rate of clearing and (2) the rate of complete disappearance of erythrodextrin in the starch substrate to measure the amylase concentration of serum and lymph, concluded that pancreatectomy had no effect upon the amount of the enzyme. In their opinion the origin of amylase was the result of tissue discard, and it appeared in the body fluids in highest concentration in the blood serum.

Elman, Arneson, and Graham (1929) have critically reviewed the previous observations concerning amylase, and the conclusions drawn from their consummation, as well as those of more recent investigators, may be briefly summarized. Much is yet to be learned which should aid in a fuller appreciation of these data and increase their clinical application.

1. The origin of serum amylase is at least in part from the pancreas.

2. There is good reason to believe that there exists a close correlation between serum amylase and pancreatic disease, particularly acute pancreatitis.

3. Deviation from normal amylase values has been reported in many diverse diseases other than pancreatitis. However, the range of these deviations is rather restricted and unlikely to be a source of diagnostic confusion.

4. Uniformity in serum amylase concentration of normal individuals has been reported by many observers using varied methods of determination. Individual normal amylase values may change but within constant limits, these limits depending upon the method of analysis employed.

5. Because of the indiscriminate chemical composition and enzyme concentration in urine and duodenal contents, amylase activity under such conditions is less constant and, consequently, as a diagnostic test less reliable.

6. Diet, vitamin deficiency, and starvation have practically no effect upon serum amylase.

7. Ligation or sudden obstruction of the pancreatic ducts leads to a prompt and marked rise in the concentration of serum amylase. Permanent and complete obstruction of the ducts results in pancreatic atrophy, and a subsequent fall in serum amylase to a point well below the normal level.

8. Complete pancreatectomy causes a permanent lowering of the serum amylase to a value one-third to one-half of its normal level.

Many additional observations concerning amylase activity have been reported. Some of these are illuminating bits of evidence which reflect the fundamental obscurities of this enzyme, its source and its structure, while the significance of other data seems to have little present bearing upon its clinical usefulness. It has been our purpose in recording 1,500 serum amylase studies in 900 representative patients to correlate the facts established by experimental investigation with the clinical factors observed both in health and in disease; to point out, if possible, the pathological conditions in which the serum amylase test is of greatest value and to determine its limits of utility and caution against its sources of error. We have performed a limited simultaneous series of studies upon urine amylase and serum lipase in an effort to compare and evaluate the virtues of these procedures. The response of pancreatic secretion to various stimulants and secretagogues, as reflected in the serum amylase level, has suggested a new and rather hopeful means of determining pancreatic function. The groundwork for such a study, beyond a few preliminary observations, is now being prepared.

METHOD

A survey of the enzyme tests as performed by the members of the American Gastro-Enterological Association (1934) revealed that only one member of that group made use of the serum amylase test. The two striking reasons given for not performing enzyme tests were (a) the inability of available methods to yield sufficiently critical data, and (b) the intricate, time-consuming nature of the tests. It has been our experience that such criticism is unjustified and, moreover, not in accord with the rather creditable reports from this country and abroad. Perhaps a more extensive use of the serum amylase test will be the means of appreciating the potentialities of this diagnostic aid.

Amylolytic activity has been measured by two general types of indirect methods. One has been based upon the activity of the enzyme in the breaking down and disappearance of starch, and the other on the accumulation of a reducing sugar formed by the enzymatic hydrolysis of starch. Stringent objections have been indicated in both categories. Using the first of these principles Wohlgemuth (1908) determined the amylolytic activity of serum by the addition of iodine to a starch substrate, thus making a colorimetric comparison possible. As the reaction progressed the starch was converted to erythrodextrin, achroodextrin, maltose, and, perhaps, glucose. The point at which the violet color yields to the brownish red of erythrodextrin is usually the end point adopted. Somogyi (1938) and others have pointed out the inherent vulnerability of this procedure—its difficulty in the selection of an end point, its lack of standardization, its time and materials consumed, and, finally, its untrustworthiness. Meyers and Reid (1933) report a plus or minus 25 per cent error in the employment of this method of procedure.

Following the ingenious work of Northrop and Hussey (1922–23), Davison (1925) and Elman and McCaughan (1927) took advantage of the fact that the viscosity of solutions decreases as the molecules dissolved in them are hydrolyzed into smaller and smaller units. Amylase activity could thus be measured by the decrease in viscosity of starch paste. The unique merits and sundry advantages of this mode of analysis cannot be gainsaid, yet the method has been found to contain a measurable source of error—namely, mixed aggregates of starch and serum protein are formed by adsorption and tend to separate out and form a sediment, resulting in a diminished viscosity. Although the nature of this inaccuracy is said to be most marked with low amylase values, nevertheless studies making use of this method must be carefully scrutinized and confirmed by a more acceptable procedure. A systematic study of enzyme activity by present polarimetric, spectroscopic, or other physicochemical means has found a limited field of usefulness outside of the experimental laboratory.

Amylase estimation by various sugar reduction methods, on the contrary, has found much favor in the literature of the last 25 years. A critical comparison of these methods and their practical application for general use has been the object of several recent important investigations. A review of this work is not within the scope of the present paper. It may be said, however, that in the cascade of amylolytic reactions starting with starch and ending in sugar production there are many obscure factors whose influence remains unknown. The velocity of enzyme activity toward different parts of the cascade is not known. The presence of activators or inhibitors as side products has not been definitely ascertained. The formation of a reducing sugar (principally maltose) may occur before much of the starch has disappeared; or, conversely, all of the starch may be converted to dextrin before any sugar is formed. Several analytical methods compute their results on the basis of a glucose standard, whereas, mostly, the reducing sugar formed by amylolytic activity is maltose.

Thus, even a cursory appraisal makes it quite apparent that there may exist many conspicuous sources of error among the several sugar reduction modes of analysis. As previously suggested, standardization of technique will undoubtedly result in more uniform amylase values and a more fundamental basis for their interpretation. Perhaps precise quantitative accuracy will be achieved only when a more direct means of enzyme isolation is created. Meanwhile the very lack of sensitiveness to serum amylase changes in diseases other than pancreatitis may be the essence of its diagnostic value in that disease.

The method employed in this investigation was first conceived in principle by McClure, Wetmore, and Reynolds (1921) and is based upon the determination of the reducing sugar formed in the enzymatic hydrolysis of starch by a modification of the Folin Wu technique. In the preparation of the reagents and the analytical procedure, however, we have observed the standards employed by Somogyi (1938),[1] and the substitution of the Folin and Wu method for the more complicated, although

[1] A detailed description of the method of analysis may be found in Somogyi's paper. The method of Folin and Wu is described in the J. Biol. Chem., 1920, 41: 367; Ibid., 1926, 67: 357; Ibid., 1929, 82: 83.

TABLE I.—AGE

Patient	Under 25 mgm. %	25–50 mgm. %	Over 50 mgm. %
1	58	80	52
2	46	75	117
3	63	52	100
4	82	100	74
5	45	91	119
6	80	105	59
7	102	86	46
8	77	119	91
9	71	98	101
10	88	49	61
Average serum amylase	71	86	82

more accurate, Shaffer-Hartmann technique was the single change that we felt justified in making. A carefully prepared 1.5 per cent starch paste was used which, by repeated test, conformed to the optimum hydrogen-ion requirement of 6.9:7.2. The starch paste was freshly prepared every 2 weeks. This precaution must not be underemphasized as it eliminates the possibility of bacterial breakdown of the starch, or the hydrolysis associated with repeated boiling. A large amount of starch is made up at one time and may be kept in a desiccator as a powder indefinitely. Thirty minutes' incubation in a water bath at 40 degrees C. was the standard time and temperature adopted. The entire procedure in both materials and method is simple and may be expediently performed in less than 1 hour. The results of amylase activity are expressed in milligrams of reducing substance per 100 cubic centimeters of serum, and values are consistently reliable up to five times the limits of normal. Saline dilution of the serum allows for determining higher values. A control blood sugar must be determined and deducted from the total reducing substance of the serum, as it is only the difference which represents amylase activity. In our experience normal values were found to range from 40 to 175 milligrams of reducing substance per 100 cubic centimeters of serum (mgm. per cent), with some slight variation beyond either limit. Lipase determinations were performed according to a modification of the Loevenhardt method as used by Cherry and Crandall (1932) and Comfort and Osterberg (1934).

RESULTS

Although the analytical procedure employed in this investigation is open to much the same criticism applied to all sugar reduction methods, yet, under carefully controlled conditions, practical experience with 1500 serum amylase determinations has minimized our sources of error and justified our confidence in the reliable nature of these results *per se*. However, the interpretation and application of these records to clinical conditions remain a matter of continued correlated study and medical judgment.

TABLE II.—AMYLASE VALUES IN COMPARISON WITH CLINICAL FINDINGS—25 FEMALES, 25 MALES

Female		Male	
Diagnosis	Amylase mgm. %	Diagnosis	Amylase mgm. %
Normal	52	Normal	75
Normal	113	Normal	113
Normal	80	Normal	91
Normal	71	Normal	80
Deaf	52	Normal	61
Peptic ulcer	49	Peptic ulcer	89
Peptic ulcer	84	Peptic ulcer	49
Peptic ulcer	67	Peptic ulcer	83
Malnutrition	74	Malnutrition	95
Hemorrhoids	50	Hemorrhoids	49
Dermatitis	62	Dermatitis	54
Hodgkin's	82	Hodgkin's	113
Tuberculosis	82	Tuberculosis	105
Pneumonia	60	Pneumonia	50
Pneumonia	71	Pneumonia	96
Hernia	74	Hernia	115
Hernia	91	Hernia	83
Hernia	60	Hernia	111
Colon cancer	50	Rectal cancer	49
Cervical cancer	72	Lung cancer	102
Breast cancer	74	Stomach cancer	73
Appendicitis	69	Appendicitis	95
Appendicitis	110	Appendicitis	63
Syphilis	85	Syphilis	56
Heart disease	61	Heart disease	58
Average serum amylase	76	Average	81

Duplicate series. A series of 20 representative serum amylase values was determined in duplicate and an average of plus or minus 7 per cent error was found to be present. The greatest deviation was 11 per cent and the smallest was zero. This degree of error is of no practical consequence and may be attributed to variations in laboratory technique.

Age. Table I represents the serum amylase values in a group of normal persons and clinic patients in which there was no reason to suspect an abnormal serum amylase level. These 30 individuals included both sexes and were unselected except for age. It would appear from these three categories that age

TABLE III.—SERUM AMYLASE ACTIVITY IN 720 PATIENTS WITH DIVERSE DISEASES

Condition	Serum amylase values						Total Patients	Aver. Amylase mgm. %
	Normal 40–175 mgm. %		High 175–275 mgm. %		Low 20–40 mgm. %			
	Number of patients	Number of Amylase tests	Number of patients	Number of Amylase tests	Number of patients	Number of Amylase tests		
Normal	16	17	0	0	0	0	16	94
Appendicitis	46	53	4	4	0	0	50	102
Cardiovascular disease	67	76	1	2	6	6	74	86
Diabetes	34	34	0	0	6	10	40	72
Gastro-intestinal disease	19	24	0	0	3	3	22	78
Genito-urinary disease	92	104	4	5	2	2	98	103
Gynecological disease	38	55	2	7	0	0	40	113
Hernia	45	68	2	3	0	0	47	83
Infectious mononucleosis	5	7	1	18	0	0	6	149
Neoplastic diseases	63	70	1	2	2	2	66	91
Peptic ulcer	23	40	2	3	0	0	25	100
Pilonidal sinus	11	13	0	0	0	0	11	94
Pneumonia	16	18	1	1	2	3	19	80
Pregnancy	4	4	0	0	0	0	4	89
Rectal diseases	22	24	2	2	1	1	25	96
Rheumatic fever	13	13	0	0	0	0	13	77
Syphilis	5	5	0	0	0	0	5	86
Thyroid diseases	26	27	0	0	2	2	28	80
Tuberculosis	4	4	0	0	0	0	4	95
Miscellaneous	125	181	1	4	1	1	127	88
							720	93

has relatively little effect upon amylase values. In general it was found that infants had a lower range of amylase activity than adults; however, although the individual variation in both was wide it remained within normal limits.

Sex. Average amylase values in a parallel group of 25 males and 25 females with comparable clinical conditions (Table II) were found to be approximately the same. The specimens used were from unselected patients in which all amylase values were within normal limits. Marked obesity in females was noted to be associated with a lowered amylase activity.

Clinical condition. In Table III there is listed the serum amylase activity of 720 patients with many diverse diseases which, for the most part, cause no serious alteration in amylase level. A few values may rise above the limits of normal and others tend to fall below. In the majority of these instances, however, repeated tests within 24 hours reveal a prompt return to normal with no subsequent aberration. We have been unable to account for these isolated, spontaneous, and transient rises in serum amylase although Friedman and Thompson (1936) have found similar elevations to occur in experimental dogs. These investigators attribute the altered amylase activity to either a functional or pathological pancreatic response. Clinically, spontaneous changes seem to bear no relation to food, drugs, temperature elevation, leucocytosis, or pain. Several amylase rises have been noted directly to follow laparotomy. It may be presumed that the intra-abdominal handling of the pancreas or perhaps the effect of the anesthesia was responsible, but we have no evidence in support of these contentions. In a small series of amylase determinations performed shortly after biliary tract operations,

TABLE IV.—SERUM AMYLASE VALUES IN 99 CASES OF GALL-BLADDER DISEASE

	Number of patients	Average amylase on admission mgm. %
Acute and subacute Cholecystitis	26	69
Cholecystitis and cholelithiasis	18	67
Chronic Cholecystitis	17	75
Cholecystitis and cholelithiasis	22	93
Choledocholithiasis	16	67

there was no constant irregularity observed. The striking expression of normal amylase levels in 94 per cent of 720 patients is a rather convincing manifestation of its stability in diseases other than pancreatitis.

Appendicitis. Among 50 patients operated upon for acute appendicitis 4 had elevated amylase values and the remainder were normal. In 2 of these patients with high levels the appendix was found to be normal by pathological examination. One may speculate as to whether a mild edematous and transient pancreatitis could be diagnostically confused with appendicitis.

Cardiovascular disease. Seventy-four patients with cardiovascular disease of varying degree were investigated. Six patients were noted as having a lowered serum amylase, and the remainder except for one to be normal. All 6 of those patients with a decreased amylase level were in severe congestive heart failure. The rôle of visceral stasis and liver and pancreatic engorgement in decreasing amylase activity has not been clearly defined, yet in studying patients with an impaired liver function we believe that such an association is in all probability more than just incidental.

Diabetes. Among 40 cases of diabetes that were observed there were both insulin treated and untreated patients. The amylase activity was depressed in 6 cases. The blood sugar levels in these particular patients were not exceptionally high, although from our records there appears to exist an inverse ratio between the blood sugar and the serum amylase. This may best be seen by a comparison of the blood sugar and serum amylase values in patients with a marked hyperglycemia.

TABLE V.—BLOOD SUGAR AND SERUM AMYLASE IN MARKED HYPERGLYCEMIA

Patient	Blood sugar	Serum amylase
1	222	102
2	268	42
3	286	47
4	236	50
5	222	100
6	236	94
7	250	60
8	400	35
9	286	34

Is the same process which apparently impairs the internal secretory function of the pancreas in diabetes also responsible for its influence upon the so called external secretory function?

Genito-urinary diseases. Ninety-eight patients with diverse genito-urinary diseases were studied in this investigation. In 4 cases the amylase was elevated and in 2 it was lowered. Terminal uremia was present in 2 of the patients having increased amylase values. Although it is generally known that amylase is excreted by the kidney, we were unable to correlate any constant serum amylase change with decreased kidney function as indicated by a moderate retention of nitrogenous products.

Gynecological disease. A mild but persistent increase in serum amylase activity was noted in 1 patient treated surgically and found to have a ruptured graafian follicle. The remaining gamut of gynecological conditions, including ovarian disease, failed to manifest any abnormal amylase values.

Infectious mononucleosis. A striking case of infectious mononucleosis was observed in which a persistent elevation of serum amylase was noted in 18 determinations over a period of 4 weeks. Following the patient's clinical recovery there was no inclination of the serum amylase to return to normal. Five additional cases of infectious mononucleosis showed no such aberration.

Peptic ulcer. Twenty-three patients with peptic ulcer were found to have normal amylase levels. Two patients were observed to have high amylase values. The first of these was a case of an acute ulcer perforating into the head of the pancreas. Probstein, Gray, and Wheeler (1938) have recently re-empha-

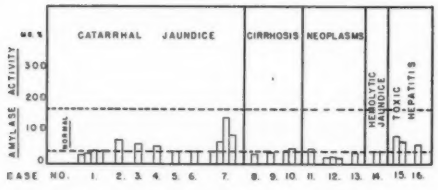

Fig. 1. Sixteen patients with liver disease showing a depressed amylase activity.

sized the association of such ulcers with increased serum amylase values and reported 4 cases in which a localized pancreatitis resulted from the perforation. Two patients in our series had a frank ruptured ulcer without involvement of the pancreas, and in both the amylase remained within normal limits.

The second patient with an elevated amylase had a chronic stenosing ulcer, and a gastric resection was performed. The duodenal stump was buttressed against the pancreas. Following this procedure the patient's early postoperative course was marked by severe vomiting and epigastric pain. The serum amylase which had hitherto been normal was now found to be elevated. Many observers have called attention to the danger of pancreatitis following gastric resection in which the pancreas is traumatized or otherwise injured by operative manipulation.

Thyroid disease. Disease of the thyroid gland produced relatively little effect upon amylase activity. No correlation could be drawn between the basal metabolic rate and the amylase level.

Miscellaneous. Minor deviations from the normal amylase level rarely occurred in a great diversity of clinical conditions. The interpretation of these isolated results was impossible. We regret that in this investigation we were unable to study patients with psychiatric, neurological, or neurosurgical disorders.

MUMPS[1]

Thirteen cases of mumps were observed in this study; 12 of epidemic mumps and 1 of surgical mumps. In concomitant serum amylase and serum lipase studies all lipase levels

[1] We are grateful to Dr. Spector and members of the Willard Parker Hospital for the privilege of observing these cases.

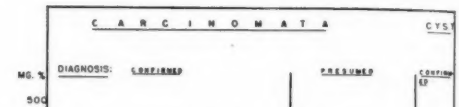

Fig. 2. The serum amylase values in 10 patients with pancreatic tumors. The pre-operative level was normal in all cases except one.

were normal, whereas the amylase was considerably elevated in practically all patients except those in whom the parotitis was unusually mild or the determination made late in the course of the disease. Orchitis and encephalitis as complications of mumps produced no effect upon the activity of these enzymes. Pancreatitis complicating mumps was not present in the diagnoses of this group. Two cases of salivary gland cysts both had normal amylase values.

DISEASES OF THE LIVER

Diseases of the liver regardless of kind appear to have a depressing effect upon serum amylase activity (Fig. 1). Sixteen patients with diverse diseases of the liver were subjected to investigation. Jaundice was the striking clinical feature in this group of cases. The diagnosis was confirmed by operation or autopsy in all of those patients having cirrhosis of the liver or hepatic neoplasms. In the neoplastic group 1 patient had a metastatic melanosarcoma and 2 patients had metastatic carcinomas; 1 from the gall bladder and the other from the rectum. Patient 15 in Figure 1 entered the hospital almost moribund with a severe yellow atrophy of the liver. The diagnosis was confirmed by postmortem examination, yet two serum amylase values taken just before death remained within normal limits.

TUMORS OF THE PANCREAS

Nine patients with carcinoma of the pancreas were observed in this study (Fig. 2). In 5 cases the diagnosis was confirmed at

either operation or autopsy and in the diagnosis was presumptive. The pre-operative amylase levels were normal in all cases except 1, patient 3, Figure 2, and in this exception a laparotomy revealed an extensive carcinoma surrounded by areas of pancreatitis and fat necrosis. Patient 1 (Fig. 2) had a carcinoma of the ampulla of vater which was resected. It is significant to note the normal pre-operative amylase level in those cases in which a tumor was resected or a biopsy taken, whereas the postoperative amylase level incident to the operative pancreatic trauma showed a marked and immediate elevation.

Apparently the slow growth of a pancreatic neoplasm is unlikely to produce the elevated amylase level so commonly associated with more sudden ductal obstruction, hemorrhage, or inflammation. Similarly, the acinar atrophy resulting from the pressure and invasion of pancreatic tumors is not sufficient to cause a striking fall in serum amylase.

One patient with a pancreatic cyst was observed after operation. An elevation of amylase occurred on one occasion shortly after operation. The results of amylase determination in this particular group of cases closely parallels a larger series of patients with pancreatic tumors and cysts reported by Wakefield, McCaughan, and McVicar (1930).

GALL-BLADDER DISEASE

Ninety-nine patients with gall-bladder disease were carefully studied both before and after operation. Table IV represents the average serum amylase values which in all categories fell within the range of low normal. However, each individual patient presented a wide amplitude of amylase variation particularly when followed for a long period of time. Thus, the interpretation of individual values must be undertaken separately if we are not to be misled by the fallacy of average statistics.

More clearly to define this position, the following histories outline the amylase level in 3 illustrative cases of gall-bladder disease.

Patient 1 entered the hospital because of chronic cholecystitis and cholelithiasis, a diagnosis made by her family physician. While in the course of pre-operative preparation the patient developed unmistakable signs and symptoms of common duct obstruction. At this time the amylase, which had hitherto been normal, increased decidedly. Shortly thereafter the patient was operated upon and a large stone was found impacted at the ampulla of Vater. Following its removal the patient's rapid clinical convalescence went hand in hand with a return to normal amylase activity.

Patient 2 had a subacute cholecystitis and cholelithiasis with normal amylase activity. At the time of operation a rather large calibered and long limbed T-tube was placed in the common duct. The serum amylase rose sharply and remained elevated until the T-tube was removed 2 weeks later. It is suggestive that the descending limb of the T-tube may have impinged upon the duct of Wirsung or, by edema, occluded it, thus causing pancreatic obstruction and a concomitant rise in amylase.

Patient 3 had an uneventful postcholecystectomy convalescence until the fourth day after operation. At this time the patient's temperature rose, jaundice was noted, pain was present, and large amounts of bile commenced to discharge from the wound. The serum amylase which had been normal on several previous determinations now rose sharply. The amylase activity of the draining bile, which is normally very low, increased markedly. Within a day or two the patient's condition was distinctly improved, however, and the amylase level of both the serum and the bile returned to normal. Shortly thereafter a small cholesterin-bilirubin stone was found in the stools which probably was responsible for the obstruction to both the common and the pancreatic ducts at the ampulla of vater.

The important studies of Millbourn (1936), Foged (1933–34), Branch and Zollinger (1938), and others have all pointed out that essentially the rise of serum amylase in gall-bladder disease depends upon the location of the stone and the anatomical interrelations of the bile and pancreatic ducts. It has been our experience that such amylase elevations are only of a moderate amplitude and are seldom to be confused with the increased amylase activity noted during the onset of acute pancreatic necrosis. Gall-bladder disease without com-

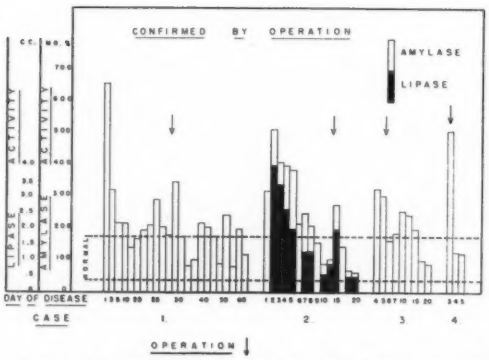

Fig. 3. The serum amylase and serum lipase activity of 4 confirmed cases of acute pancreatitis. The highest level occurs early in the course of the disease.

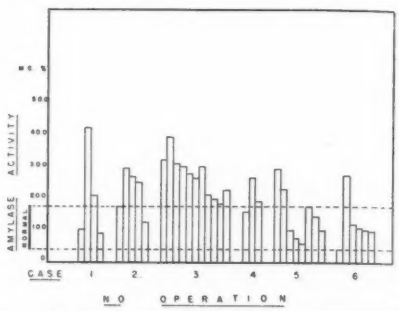

Fig. 4. Six patients in whom the serum amylase values were increased. The clinical diagnoses were in doubt although presumptive opinion based upon amylase studies favored pancreatic involvement.

mon-duct stones rarely gives abnormal amylase values.

ACUTE PANCREATITIS

Four patients with acute pancreatitis, the diagnosis confirmed at operation, were observed in this investigation. The amylase activity in all of these cases (Fig. 3) and the lipase activity in at least one of them were intensely increased. Concomitant urinary amylase determinations were found to have a greater range of daily fluctuation but, in general, to corroborate the serum amylase level. A lag of 24 hours was frequently noted in the urinary amylase value when compared to that of the serum amylase.

The serum amylase response reaches its peak within the first 48 hours of the disease and may fall rapidly, if not precipitously, within the next few days. Thus, the diagnostic value of the amylase test is limited to the early course of the disease, but it is precisely at this time that it is of greatest benefit in the differential diagnosis of the acute abdomen. Practically all observers agree that significant serum amylase elevations occur regardless of the nature or severity of the pancreatic lesion. In our investigation patients 2 and 3 represented the milder acute edematous type of pancreatitis, whereas patients 1 and 4 were representative of the more fulminating forms of acute pancreatic necrosis; however, a marked serum amylase rise was present in both groups of patients.

Patient 1 (Fig. 3) suffered a prolonged period of retarded convalescence which was more or less indicated by the fluctuating postoperative amylase values. Dragstedt, Haymond, and Ellis (1934) have called attention to this condition of pancreatic cachexia, probably the result of extensive damage to the pancreas, and have suggested substitution therapy—particularly the internal secretory enzyme lipocaic. The rapidity with which the serum amylase level returns to normal in cases of acute pancreatitis may serve as a presumptive prognostic sign in predicting the extent of pancreatic destruction.

The secondary rise in serum amylase following operation (Fig. 3) appears to have been the result of surgical manipulation and maneuvers designed to insure pancreatic decompression. Principles of pancreatic appeasement based upon surgical therapeutic procedures are not founded upon the exact anatomical consideration of the pancreatic capsule and its lobular extension. The more general acceptance of the serum amylase test as a reliable aid in the diagnosis of acute pancreatitis has in part been responsible for the recent tendency to treat this disease conservatively.

In our limited experience with the serum lipase test we have noted that its activity parallels that of the serum amylase in all of the pancreatic diseases. Its aptness to remain elevated for a longer time has been noted by others; but the fact that its performance takes 24 hours seriously handicaps its practical usefulness in clinical emergencies.

BILIARY TRACT DISEASE

The unconfirmed diagnoses of the patients represented in Figure 4 varied from postcholecystectomy syndrome and biliary dyskinesia to pancreatic reflux and chronic pancreatitis. From the clinical history and amylase studies of these patients it is not unlikely that the responsible locus might very well have been a pancreatic lesion. The experimental work of Archibald (1919) and Wangensteen, Leven, and Manson (1931) supports the opinion that transient states of pancreatitis may be produced by pancreatic reflux in the course of a disturbance of the normal function of the sphincter of Oddi. The investigations of Cole (1938) and Elman (1937) add clinical confirmation to this conception and reaffirm the diagnostic value of the serum amylase test in acute edematous pancreatitis. The obscurity of the clinical signs and symptoms in this group of cases constitutes a diagnostic hazard, and, were it not for enzyme determinations, many patients with acute edematous or interstitial pancreatitis might continue to be clinically unrecognized.

CONCLUSIONS

1. Age, gender, diet, vitamin deficiency, and starvation have practically no effect upon serum amylase values.

2. Normal serum amylase levels range within constant limits when determined by a reliable method of analysis.

3. Because of the indiscriminate chemical composition and enzyme concentration in urine, feces, and duodenal contents, amylase activity under such conditions is less uniform and, so, as a diagnostic aid less trustworthy.

4. Ninety-four per cent of 720 patients having clinical conditions other than mumps or diseases of the biliary system were found to have normal serum amylase values.

5. Patients with mumps were observed to have elevated amylase levels.

6. Patients with liver disease, regardless of kind, often have depressed amylase activity.

7. Deviation from normal amylase values occurs infrequently in diseases other than pancreatitis. The range of this aberration is rather restricted and unlikely to be a source of diagnostic confusion.

8. A prompt and significant rise in serum amylase activity occurred in 4 cases of acute pancreatitis in which the diagnosis was confirmed and in 6 similar cases in which the diagnosis was presumptive. The amylase elevation reaches its peak within the first 48 hours of the disease and usually returns to normal several days thereafter.

9. The serum amylase determination is a most helpful and reliable aid in the diagnosis of acute pancreatitis, particularly if this disease is to be treated conservatively.

I am most grateful to Dr. H. Stine and Miss Weinreb for their laboratory assistance and to Dr. E. Fishberg for her helpful interest and counsel.

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CANCER OF THE RECTUM AND RECTOSIGMOID

Its Surgical Treatment

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THE *annals of medical history* record many and varied procedures of diagnosis and treatment for cancer of the rectum. Historical data on surgery as far back as the Hippocratic era mention rectal operations. True, most of these procedures were for fistulas or hemorrhoids but occasionally one reads of cauterization operations for tumors which obviously were malignant. Beginning with these primitive maneuvers surgery for rectal cancer steadily progressed from local operations to abdominal drainage procedures and finally to a combination of colostomy and removal of the rectum which culminated in the modern combined abdominoperineal operation in one and two stages.

A brief review of some of these historical data which mark this evolution is interesting and is put down here in the belief that one should not lose sight of the efforts of pioneer surgeons in the present day atmosphere of standardization.

Surgical intervention for cancer of the rectum was first proposed by Morgagni at the beginning of the eighteenth century, but not until 1739 was the initial operation, a form of posterior proctectomy, undertaken by Faget.

It was not until nearly 100 years later that the procedure was again attempted by Lisfranc, who in 1826 performed his first successful posterior resection for carcinoma of the rectum. In 1829 his pupil, Pinault, published a thesis in which he reported 9 cases and, therefore, credit is usually given Lisfranc for laying the foundation of radical surgical removal of the rectum for cancer. Be that as it may, these early procedures were pitifully inadequate, for during this period the operation was merely a circular amputation of the anal canal leaving a troublesome incontinent perineal anus, and as we now know from a slow and painful accumulation of 200 years' experience, a fertile field for early recurrence in the bountiful supply of regional lymphatics.

Dieffenbach and Velpeau continued to forge ahead in the face of discouraging mortalities by adding minor variations to the original procedure. Amussat, the first to remove the coccyx, was followed by Verneuil in 1873, who adopted coccygectomy as a routine procedure because of the more satisfactory exposure afforded.

Kocher, in 1876, not only excised the coccyx, but removed a portion of the sacrum for the same reason. Gradually a realization of the importance of a more and more radical extirpation forced itself upon the minds of these courageous pioneers. Next on the roster of famed surgeons who devoted their skill and ingenuity to the ever widening problem of cancer of the rectum comes the name of Kraske.

In 1885 before the Fourteenth Congress of German Surgeons, Kraske presented his great contribution to the advancement of the surgical treatment of malignant disease of the rectum. The magnitude of his contribution can be judged only in the light of his time, for it combined two features of the greatest importance: (1) a most radical removal of the rectum well up to the peritoneal reflection through an approach which sacrificed a portion of the sacrum, as well as the coccyx, and (2) conservation of the sphincteric mechanism.

During the next quarter of a century such men as Hochenegg, Bardenheuer, Billroth, Rehn, Rydygier, Schelky, DePage, Hartmann, and others suggested many modifications which met with small popularity.

Perhaps the greatest single adjunct to radical removal of the rectum is the simple procedure of colostomy which far antedated even the earliest attempts at proctectomy. It has, down through the ages, paralleled the development of extensive rectal surgery, but not until well along in the nineteenth century have the two become amalgamated as basic principles in this field of endeavor. Colostomy was first recorded by Aurelianus, as having been performed by Prazagoras 400 years before Christ in an attempt to treat ileus, but the bowel was closed after having been evacuated of its contents.

Littré, in 1710, through the medium of a child who died of a congenital obstruction of the rectum, conceived the idea of a permanent colostomy. He was followed in this by Pillore and DuBoise, but not until 1793 did Duret perform a left iliac colostomy on a child with an imperforate anus. Pillore, in 1776, performed a cecostomy for rectal cancer, but it is the French surgeon, Amussat, to whom we are indebted for establishing the

principle of colostomy in the presence of cancer of the rectum. In 1839 he observed a patient dying of obstruction from rectal cancer and was thereby convinced of the desirability of colostomy, which he termed a grave but not insupportable infirmity. Amussat developed the lumbar colostomy, and during the next 15 years Baudens, Keyworth, and Phillips improved on the operation.

In 1865, Ward advocated routine lumbar colostomy in all cases of rectal cancer, so that gradually the maneuver became recognized as an integral part of the operative plan of treatment. The principle of multiple stage operation was thereby established, and henceforth, development has progressed hand in hand with anesthesia and aseptic surgery to culminate in the most courageous endeavor in this field, the combined abdominoperineal resection of the rectum.

As is often the case, progress has been the stepchild of error and so it was in 1883, when Czerny performed the first single stage perineo-abdominal resection of the rectum. He found it impossible to remove a carcinoma well up in the rectum or rectosigmoid through the perineal route as intended, so he promptly opened the abdomen to complete the resection transperitoneally.

In 1887, von Volkmann published his work on the combined abdominoperineal operation, which by the turn of the century was not only vigorously championed but considerably improved upon by Miles.

During the past 30 years the tangled web of surgical endeavor in this field has, through the ingenuity, skill, and multiplicity of ideas, culminated in the development of a number of operative procedures, the worth of which it has taken valuable time and experience to prove or disprove.

The procedure which represents the most radical attempt at extirpation of rectal cancer with block dissection of the gland bearing tissues represents the ultimate in radical surgery in this location. It is a tribute to Miles that most experienced operators of today recognize the importance of the fundamentals of his operation and after practicing various types of modification, they gradually are coming more and more to his original procedure. The modifications have been popularized largely by Pauchet in France, Lahey in this country, and Gabriel and Grey Turner in England.

The operation of Miles, with minor variations, has stood the test of time and in the hands of many surgeons is recognized as the operation of choice, when, of course, the indications for its use have been fulfilled. The efficacy of the one-stage procedure must not, however, be permitted to overshadow the distinct advantages of the graded operation for those who fail to meet the requirements of the more radical maneuver.

In the discussion of carcinoma of the rectum it must be pointed out that for three reasons it has become a problem of enlarging interest and importance during the last half century. First, there is a steady increase in the number of our population who, during the past 50 years, are reaching well beyond what has been popularly referred to as the "cancer age" (40 to 70 years). For example, life expectancy has been increased by 20 years during the last 8 decades, to attain the average span of 60.5 years. Second, the great wave of popular interest stimulated by educational programs and propaganda fostered by such worthy organizations as the Society for the Prevention of Cancer, and others, has created a cancer consciousness which impels people to seek early medical attention. Finally, and perhaps most important of all, are the vast strides which have been made in diagnostic facilities during the same period.

It has been suggested that the incidence of cancer of the rectum may be on the increase. In England and Wales statistics have shown that during the period from 1920 to 1929, the mortality from cancer of the intestine including the rectum, has increased from 6.8 to 13.6 per hundred thousand. In this country during the same period the figure has increased from 7.1 to 9.4 deaths per hundred thousand. The significance of these figures is obvious, provided this is an actual and not a relative increase dependent upon the progressive efficiency and increasing accuracy of the Bureau of Vital Statistics.

With regard to the racial distribution of cancer of the rectum, sufficient data have not been accumulated to permit of an accurate estimation. Raiford observed at the Johns Hopkins Hospital that the ratio of malignant disease of the colon in white and colored patients was about 8 to 1. In my series of 424 cases of cancer of the colon and rectum seen during the past 5 years, only 3 patients were colored—an incidence of 0.007 per cent. Of 215 patients suffering from carcinoma of the rectum and rectosigmoid only 1 of these was colored. It is generally conceded that carcinoma of the rectum occurs more frequently in men than in women. In a series of 300 cases reviewed by Rankin and Jones, the proportion of men to women was about 3 to 2, although Pfeiffer, Gabriel, and others find it to be nearer 2 to 1.

Rectal cancer is no respecter of age, although it usually occurs in patients between the fifth and

eighth decades of life. In a series of 7,313 collected cases of carcinoma of the rectum, Pennington found that 3.7 per cent of these patients were 30 years of age or less. In a similar series of 1,452 cases reported by Rankin and Comfort, 3.8 per cent were found to occur in patients under 31 years of age.

In the literature a total of 25 cases of cancer of the large bowel have been reported in patients less than 18 years of age, and of these only 5 were situated in the rectum.

GENERAL CONSIDERATIONS

Etiology. The etiology of cancer of the rectum as of carcinoma elsewhere in the body is still a matter of speculation. Rosser has suggested the importance of benign anorectal lesions as a precursor of malignant disease. Ewing, however, is not of this opinion. Likewise, Pennington and Jones feel that such lesions, although they are not infrequently associated with anorectal malignancy, have rarely if ever been proved the cause.

The rôle of trauma, which undoubtedly plays a part in the predisposition to malignant disease elsewhere in the body, has been viewed with suspicion because it is the rectosigmoidal vestibule, the commonest site of cancer of the large bowel, which is subjected to the effects of a change from semisolid to formed stools. Reasoning thus, however, the effect of constipation, far more commonly a feminine failing, should, if an important factor, reverse the ratio in frequency of carcinoma of the rectum between men and women, which as previously mentioned is about 3 to 1. The anal canal moreover is subjected to far greater trauma than any other part of the lower bowel, yet it is the most infrequent site of carcinoma.

The relation of polyposis to cancer of the rectum was first noted by Cripps, who in 1882 observed the familial tendency of the lesion and the frequency with which these cases developed carcinoma. Hansford concurred with Cripps in his feeling that polyps were a precursor of cancer of the colon, and later Bardenheuer and Landel presented histological evidence of the malignant transformation of these polyps. Many other observers have established this thesis although it cannot be proved that all cancers of the rectum arise from polyps.

Pathology. The intimacy with which the gross and microscopic pathology of malignant lesions are associated with the prognosis of an individual or group of cases has through the years been more and more emphatically impressed upon the surgeon. The evolution of this relationship can be traced through generations of the closest co-operation between surgeon and pathologist and through constant effort the fundamental principles of radical surgical extirpation have been developed.

Dukes, of London, has by means of a careful examination of gross specimens with regard to depth of penetration in the bowel wall established an index of malignancy upon which he is able to gauge prognosis. Broders' prolific study of the microscopic characteristics of malignant lesions upon which he has based his work of grading the activity of neoplastic tissue has, likewise, proved an extremely reliable index by which to judge prognosis. He has observed that the more nearly the cellular elements of a new-growth approach the embryonic or undifferentiated type of tissue, the more malignant the lesion, and by the same token, the more closely these cells resemble the cellular elements of normal tissue, the lower the degree of malignancy. Having established a numerical ratio between the early and the late forms of cells, he has quartered this relationship in order to express the degree of malignancy in four grades, the first being the least, while the fourth is the most malignant.

With the exception of an occasional squamous cell carcinoma at or about the anal margin and the very rare occurrence of such a lesion arising from the rectal mucosa, the remaining carcinomas are of glandular origin. All cancers of the large intestine are said to arise fron Lieberkuehn's glands. To explain the appearance of a squamous cell carcinoma developing from the mucosa, it has been maintained that regenerative cells of the glandular epithelium have the ability to produce either a secretory (glandular) or protective (squamous) epithelium.

Briefly the types of rectal carcinoma are referred to by the following descriptive terms which suggest the gross characteristics of the lesion: (1) medullary adenocarcinoma; (2) scirrhous or fibrocarcinoma; (3) mucoid or colloid adenocarcinoma; (4) papillomatous carcinoma; (5) squamous carcinoma, and, finally, (6) the melanoma, which has been variously described by some as sarcoma and by others as carcinoma. Biopsy serves to substantiate the diagnosis which can nearly always be made by palpation and visualization. However, it must be emphasized that a negative biopsy should never be taken as conclusive evidence of benignancy in the presence of a suggestive lesion.

Anatomy. There is some controversy in regard to the relative frequency of involvement of different portions of the rectum and rectosigmoid. Because of the relative ease with which a rectosigmoidal growth may prolapse into the ampulla

of the rectum, the proctoscopist is often misled as to the actual location of the lesion. The rectosigmoidal juncture may, on the mucosal surface, be marked by a clear cut line of demarcation or the transition may be so gradual that a segment 2 to 3 inches long is involved. For the sake of simplicity and accuracy the rectosigmoid has been considered to lie beneath the peritoneal reflection of the bowel and include the lower inch of the sigmoid and the upper inch of the rectum.

Edwards reports that about 80 per cent of the growths are situated within 5 to 7.5 centimeters of the anus. Grant reviewed 100 cases to find half were located in the rectum and half in the rectosigmoid. Kraske believed the rectosigmoid to be the commonest site, while in a series of 100 cases studied by Rankin and Graham, 69 were found at the rectosigmoid, 29 in the rectum proper, and 2 in the anal canal. Pennington observed that of 926 cases of nonannular growth, 547 occurred on the anterior wall, 280 on the posterior wall, and only 99 were situated on the lateral walls.

Of greatest importance in the problem of cancer of the rectum and rectosigmoid is the lymphatic drainage of this portion of the lower bowel, and in the last analysis it is our knowledge of this subject upon which rests the choice of operative procedures. First to recognize the full significance of the regional lymphatics with regard to surgical extirpation of the rectum and rectosigmoid for malignant disease was Miles. In a detailed study of the problem he has clearly illustrated the avenues of metastatic invasion. The rich submucosal and intramural lymphatic plexuses drain into an arborization of lymphatic channels which culminate in a trunk at the mid-portion of the inferior mesenteric artery. He observed that cancer cells may spread upward, downward, or laterally in this network and that the entire perirectal supportive structures and connective tissue as well as the rectosigmoidal mesocolon were a potential source of metastasis. Gabriel, Dukes, Bussey, and others have further emphasized the importance of radical removal of all the node bearing tissues, but the painstaking and laborious work of Gilchrist and David has proved beyond a shadow of a doubt the futility of anything other than the most radical extirpation. From a study of 47 specimens of cancer of the rectum removed by the Miles technique they showed that in 68 per cent metastatic nodes were present. The specimens contained an average of 52 glands each, but the size of the growth and the duration of the symptoms had no relation to the number invaded, and they showed that by means of microscopic examination alone could the presence of malignant tissue be determined. Palpation and gross examination were notably unreliable. They also observed, as did Miles, that with lymph blockage above the tumor, retrograde metastases were found below the growth, while in lesions situated near the levator ani, metastasis along the muscle sheaths was not uncommon. It was also their contention that as squamous carcinoma of the mucocutaneous junction metastasized to glands along the superior hemorrhoidal artery as well as to the inguinal glands, radical resection of the rectum is indicated.

Symptomatology. The early diagnosis of cancer of the rectum and rectosigmoid depends upon the presence of signs and symptoms, the intelligence of the patient, and the alertness of the attending physician. Wherein lies the discrepancy which permits of 9 to 13 months' duration of symptoms before operation, it is difficult to determine. No less tragic, however, is the incidence of hemorrhoidectomy performed on patients suffering from cancer of the rectum during or after which operation the actual diagnosis is made. Jones had reported an incidence of 25 per cent in a large series of cases referred to him for operation.

Just how long after the appearance of a lesion is required for the onset of signs and symptoms is not known, but it is highly probable that from 2 to 3 months is sufficient time. In a series of 1,234 cases, Newman found the average duration of 13.1 months between the onset of symptoms and the diagnosis of carcinoma in this portion of the large bowel. In 300 cases Rankin and Jones found it to be 11.7 months, while Brindley in 167 cases reported 9.4 months.

The signs and symptoms of rectal or rectosigmoidal cancer may vary with the individual, but commonest of the early manifestations are the passing of blood and change in bowel habit. The appearance of blood in or on the stool is not, however, a very early symptom in the course of the disease because sufficient time must have elapsed for the lesion to have penetrated the mucosa with resulting ulceration. It may vary in quantity from scant streaking to actual hemorrhage, which has not infrequently proved to be the presenting symptom. In my series of 539 cases, bleeding was found to be present in 89.5 per cent, while in nearly one-third of the group it was the earlier manifestation of disease. Buie, in a study of 1,937 cases of cancer of the rectum and sigmoid, reported bleeding in 84 per cent, Brindley 80 per cent, and Rosser 78 per cent.

Change in bowel habit is perhaps the commonest early symptom of rectal and rectosigmoidal

cancer, and in my series.75 per cent of those patients suffered this initial complaint. Constipation was noticed in 55 per cent, while 20 per cent suffered from diarrhea. Rosser reported that 61 per cent complained of constipation, while 22 per cent were affected with diarrhea. Constipation may be and often is a result of the obstructing tendency of the lesion; however, Miles contends that there is a functional inertia of the bowel which fails to respond readily to medication and is only rarely associated with distention. Pain, excessive weight loss, weakness, and anemia are all late manifestations of far advanced disease for which only palliative surgery can be done.

Diagnosis. In the diagnosis of cancer of the rectum and rectosigmoid only two simple procedures are necessary. Well over 50 per cent and probably almost 80 per cent of all lesions in this portion of the bowel may be reached by the examining finger. The remainder may be visualized with little difficulty by means of the proctoscope. Available then to every practitioner is this first procedure, while the proctoscope, even in the hands of the unskilled, is not a dangerous instrument when introduced under direct vision. There have, however, been reported cases and doubtless many times more unreported cases of rectal injury or perforation at the hands of the overenthusiastic proctoscopist. Gentleness is the prerequisite of successful proctoscopy. Palpation or visualization will nearly always substantiate the diagnosis because of the characteristic appearance and feel of such lesions, but doubt may be quickly dispelled with a biopsy. It must be remembered, however, that a negative biopsy is of no significance.

Pre-operative preparation. Having once established the diagnosis of malignant disease of the rectum or rectosigmoid, by no means a small part in the care of these patients is the pre-operative preparation which usually requires from 5 to 7 days. General physiological rehabilitation is brought about by means of a well balanced, non-residue, high caloric diet, supplemented with fruit juices, sugar candy, and vitamin concentrates. Anemia if present is combated by transfusion. A daily fluid intake of about 3,500 cubic centimeters is encouraged, and such laboratory procedures are performed as deemed necessary in the determining of the physiological reserve of these patients. The importance of cleansing the colon cannot be too emphatically stressed, hence the desirability of the non-residue diet. The bowel is washed morning and evening with repeated high irrigations of salt solution until the fluid returns clear. The day before operation enemas are discontinued and paregoric is given to allay peristalsis.

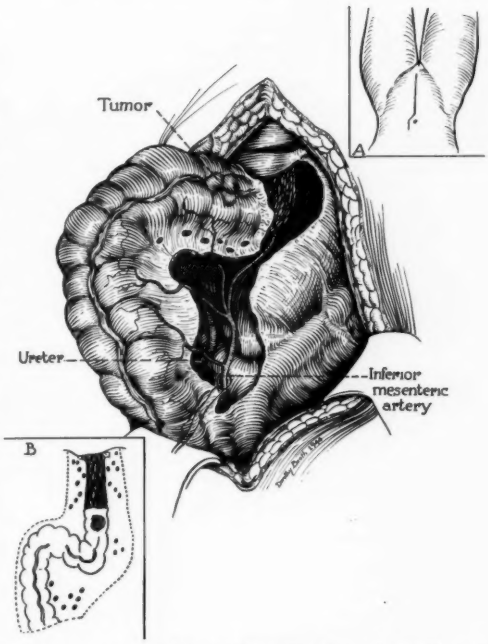


Fig. 1. A, The low mid-line incision. B, location of tumor, the distribution of the lymphatic supply, and the segment of bowel to be removed. The center drawing shows anatomical structures after the completed dissection of the pelvis. The point of ligation of the inferior mesenteric artery is indicated. The location of the tumor at the rectosigmoid juncture which is the commonest location is shown. The right lateral parietal peritoneal flap which will form a part of the new pelvic floor is demonstrated.

CHOICE OF OPERATION

In the treatment of cancer of the rectum and rectosigmoid the ultimate aim is to offer the most radical maneuver possible to the greatest number of patients. As has been proved by the work of Gabriel, Dukes, and Bussey, David and Gilchrist, only the most widespread removal of gland bearing tissue can be considered as a minimal procedure if a high ultimate curability figure is to be the goal of our endeavor.

In order to fulfill this dictum, therefore, such operative procedures as the combined abdomino-perineal or perineo-abdominal resection must be considered as first choice. Surgical limitations, however, exclude an appreciable percentage of cases which must, therefore be subjected to a less formidable procedure.

The Lockhart-Mummery procedure more nearly incorporates the desirable features of the combined operation than any of the other methods

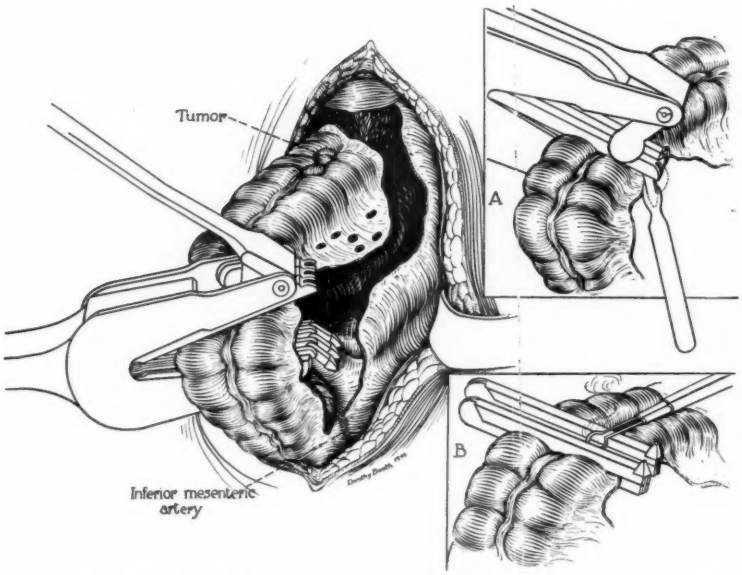


Fig. 2. The division of the bowel and the application of the Cope modification of the DeMartel clamp. A, The clamp being closed with its three clips in place. The center clip is removed and the bowel is cut with a cautery between the other two, as in B.

and must therefore, be considered the procedure of choice for this second group. Neither local destruction of the cancer nor preservation of the sphincteric mechanism by segmental removal can have any effect upon the metastatic node bearing tissues, and although there may be an occasional indication for one of these procedures they can receive scant favor.

In a recent publication I have enumerated the advantages of the one-stage combined abdominoperineal operation which are as follows: (1) It conforms to the principles of radical extirpation of cancer elsewhere, removing the local growth and tissues in the zones of spread; (2) it permits of variations and modifications to be done in either one or two stages; (3) it may be accomplished either as an abdominoperineal or as a perineoabdominal operation; (4) with increasing experience on the part of the surgeon, the operability curve may be broadened and at the same time the hospital mortality remain below 10 per cent; (5) 5 year end-results from the clinics of the most experienced advocates of the radical combined procedures indicate a higher percentage of 5 year cures than for the other types of operation; (6) only one laparotomy is required, so that time and expense are saved for the patient; (7) the blood supply to the growth may be ligated before the pelvic dissection is undertaken; (8) the procedure is applicable to all ampullary and rectosigmoidal cancers; and (9) the mortality differs very slightly from that of perineal excision when operability curves are taken into consideration.

The combined abdominoperineal operation. The abdomen is opened in the lower mid-line extending the incision slightly above the umbilicus and to the left in order to give adequate exposure. The abdomen is quickly explored from above downward. The surface of the right and then the left lobes of the liver are palpated for metastatic nodules and the exploring hand is passed down along the course of the aorta to determine the presence of glandular involvement. The pelvis is then examined and finally the growth itself is gently palpated to determine whether or not it is operable. In the favorable case the table is then placed in a moderate Trendelenburg position, a self-retaining retractor is fixed in place, and the small bowel is packed well into the upper abdomen.

The sigmoid is then freed from the left pelvic brim where it is frequently attached by the parietomesenteric reflection of the peritoneum. The inferior mesenteric vessels are then clamped, divided, and double ligated just distal to the left colic artery thereby leaving adequate vasculariza-

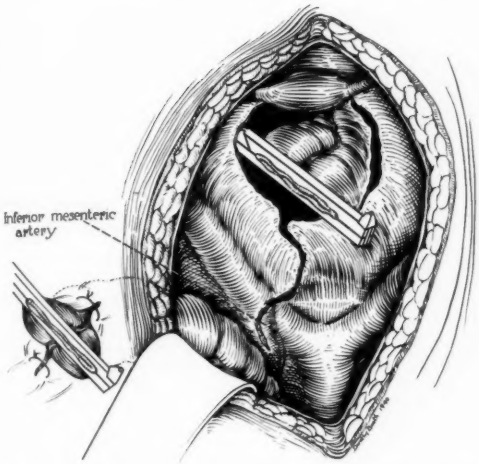


Fig. 3. The completed operation and newly manufactured colostomy in the left groin. The pelvic floor has not been completely closed. The opening here exhibits the severed end of the segment to be removed which is to be dropped back retroperitoneally. The two parietal peritoneal flaps are snugly closed to form the new pelvic floor and the uterus and broad ligament are used as additional support if the patient is a female.

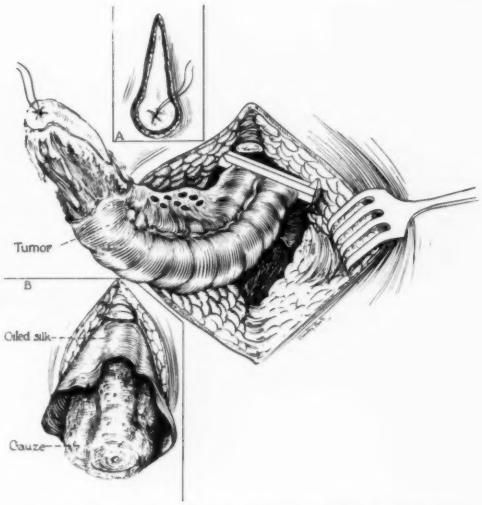


Fig. 4. The posterior part of the operation. A, The type of incision. The main drawing demonstrates the completed operation with the segment to be removed in process of extraction. B, The pelvic cavity filled with a gauze pack which is encased in oil silk. A few sutures loosely close the wound over the coccyx.

tion of the upper portion of the sigmoid from which the colostomy is to be fashioned. The peritoneum covering the left side of the rectosigmoidal mesentery is then incised, and the incision is carried well down into the pelvis, but parallel to the bowel. The parietal peritoneum is then dissected free from the brim of the pelvis and downward, thus exposing the left ureter and iliac vessels. The bowel is then retracted to the left, again the peritoneum is divided well up on the mesentery and the incision extended down into the right pelvis parallel and close to the bowel. The parietal peritoneum is then freed up and the rectovesical fold in the male or the peritoneal floor of the pouch of Douglas in the female is divided and the anterior wall is dissected free. The bowel is then held forward, the hand is placed in the hollow of the sacrum, and by means of blunt dissection the upper portion of the rectum is mobilized. At this point the mesentery of the bowel is completely divided and by means of the ingenious clamp devised by DeMartel and modified by Cope, the bowel is divided with the actual cautery. Care is taken to apply the clamp at a well vascularized portion of the sigmoid, and there is left a sufficiently long segment with which to fashion the colostomy. The pelvic dissection is then carried well down behind and lateral to the rectum so that all the gland bearing tissue is removed with it. The middle hemorrhoidal vessels are divided and ligated. The distal portion of the bowel is dropped into the pelvis and a new pelvic floor is made by the approximation of the lateral peritoneal flaps. In the female this step is somewhat easier than in the male because a portion of the broad ligament and uterus may be utilized.

A suitable site in the left groin is now chosen for the colostomy and at this point a circular area of skin 3 centimeters in diameter and including the subcutaneous fat is excised. The underlying muscles and fascia are then divided down to the peritoneum which is opened. The DeMartel clip on the upper segment of the sigmoid is then passed through this opening and the bowel is drawn gently but snugly into place. One or two sutures may be used to approximate the wound edges, but the bowel is never sutured to the abdominal wall. The clip is left in place for 36 hours.

The omentum is brought well down over the small intestine and the midline incision is closed in layers, dressings are applied, and the patient is turned on his abdomen with the hips moderately elevated.

The second half of the operation is then carried out after the snug closure of the anus with a

strong linen suture. Two concave incisions extending from the sacrococcygeal junction to the midportion of the perineum are made to include the anus and a generous portion of peri-anal skin and subcutaneous tissue. The levator ani muscles are divided well laterally and much of the peri-rectal fat is removed. The supporting ligaments of the rectum are divided and the coccyx is excised. Having once established a line of cleavage between the rectum and the prostate or in the recto-vaginal septum, dissection is carried out without difficulty. The entire portion of the lower bowel is then removed with ease. After bleeding is controlled, a sheet of oiled silk 2 feet square is placed over the posterior opening and invaginated into the depths of the pelvic cavity by means of two large gauze packs introduced with sufficient pressure to give support to the pelvic floor. The wound is partially closed with several stay sutures of silkworm gut, and a snug dressing is applied in such a manner that the buttocks are pressed firmly together.

Postoperative treatment. Equally meticulous attention is required during the postoperative course of these patients, and it has become my routine to give all patients in whom the bowel has been resected a transfusion of 500 cubic centimeters of citrated blood immediately after operation. Parenteral fluids to the amount of 3,500 cubic centimeters are administered daily for the first 3 days, and thereafter fluids by mouth are given in gradually increasing quantities. The patients are kept in a warm room and turned hourly until they react and thereafter every 2 hours for 24 hours. Carbon dioxide is administered routinely and adequate sedation is essential. The colostomy clip of the DeMartel clamp is removed after 36 hours, at which time the first of the two packs is removed from the posterior wound. The second is removed 24 hours later, and irrigations are begun the following day. The patient is usually allowed up on the twelfth to the fourteenth day and sitz baths are started immediately. The average duration of hospitalization following the combined abdomino-perineal operation is 28 days.

OPERABILITY, MORTALITY AND PROGNOSIS

In the evaluation of any surgical endeavor the personal equation of the operator must be taken into consideration. In order to introduce this highly important factor, statistical data must include an expression of two intangibles, that is, surgical judgment and technical skill. This can be accomplished only if, in a group of patients, the percentage of operable cases is co-ordinated with the mortality rate and end-results, for if only a few carefully selected individuals are subjected to operation, the mortality and end-results of this group will present a highly creditable figure; however, the remainder of the group will be afforded scant opportunity of recovery. In order to increase the availability of operative treatment the percentage of cases subjected to radical surgery must constantly be raised, while the mortality is kept as nearly fixed as possible. Only judgment and skill may widen the curves of this graph, and with their divergence end-results will take care of themselves.

It is encouraging to note the gradual increase in operability figures both in this country and in England and the Continent. Gabriel at the St. Mark's Hospital, London, has increased his operability for the decade of 1921 to 1931 by more than 20 per cent of the preceding ten years. On my service between 1925 and 1930 the figure remained close to 50 per cent, while during the 5 year period ending 1939, I have been able to operate on 75 per cent of these patients without, however, increasing the mortality to an unreasonable figure.

Table I includes patients seen in my private practice during the past 5 years. The trend of my service tends to parallel that of many of my colleagues in that more and more often we are able to use the one-stage combined abdomino-perineal operation which is unquestionably the most radical procedure available for the treatment of carcinoma of the rectum and recto-sigmoid. The mortality rate, however, has not suffered through increasing the applicability of the procedure. Although fewer two-stage procedures are being performed, they are reserved for the poorer surgical risk, and I feel that the horizon of the Lockhart-Mummery maneuver, colostomy, and subsequent posterior resection, is being extended to include more of this group than has been my wont in the past.

TABLE I.—OPERATIONS FOR CANCER OF THE RECTUM AND RECTOSIGMOID

	Cases	Deaths	Mortality Per cent
One-stage	112	7	6.2
Colostomy and posterior resection	41	3	7.3
Colostomy alone or with exploration	42	6	14.2
Exploration alone	10	0	....
Two-stage resection (Rankin)	7	0	....
Cecostomy (acute obstruction due to cancer)	3	1	....
	215	17	

Patients	215	Resections	160
Operations	260	Resectability	73%

It is interesting to note that in this series of 112 combined abdominoperineal resections there have been 7 deaths, a mortality of 6.2 per cent, whereas, in a group of only 41 Mummery resections there have been 3 deaths, a mortality of 7.3 per cent, perhaps a little high, but with an operability figure of 75 per cent obviously many of the graver surgical risks are being afforded the opportunity of resection who would otherwise perish. It must be observed that in the evaluation of the results of this two-stage procedure the mortality following colostomy in patients who at that time were thought to be resectable, is included with the mortality of the second stage, whereas the mortality on the single-stage combined operation is in itself a true figure.

In those patients upon whom colostomy alone is performed the mortality is still higher, 14.2, and justifiably so because it is only in the last stages of disease that they present themselves. It is difficult to countenance the tendency of some who feel that colostomy in the nonresectable cases should be withheld until obstruction is actually present. Today, as in 1839, the principle of colostomy as part of the plan of treatment of cancer of the rectum established by Amussat, is still unchanged, and when it is performed earlier in the course of the illness the misery, pain, and profound toxemia incident to obstruction may be prevented. More and more the prejudice against colostomy is being overcome. Few surgeons there are who will not now admit the desirability of colostomy, and change in the attitude of the general practitioner is more encouraging.

The statistics presented by Dr. D. F. Jones in 1936 are a good illustration of what may be done by the hand of a master surgeon. In a series of 672 patients 63.5 per cent were operable. In this group 165 were subjected to the one-stage combined abdominoperineal operation with a mortality of 13 per cent, and a 52.6 per cent five year cure. In 110 two-stage combined operations the mortality was 27 per cent and the five year cures reached 51.5 per cent. Mummery reported a series of 330 cases upon whom he performed the colostomy and posterior resection with a mortality of 7 per cent and a five year cure of 52 per cent. In this series there is no operability figure.

Gabriel has steadily increased his operability rate until for the year 1936 it had reached 67.8 per cent. His mortality in 100 perineal operations from 1933 to 1936 was 5 per cent, while only 37 to 40 per cent of these patients were living and well at the end of five years. In 100 patients operated on by the one-stage combined abdominoperineal operation 22 died. End-results were not tabulated.

Miles in several isolated series of cases has decreased the mortality in his procedure from 25 per cent to 7.6 per cent. He reported a 73 per cent 5 year survival in a series of patients operated on from 1920 to 1925, while Abel, of London, reported a 5 year survival of 69.3 per cent following the one-stage combined abdominoperineal operation, calculating as did Mummery and Gabriel. In 151 combined abdominoperineal resections in one stage, T. E. Jones reports that he had a 10.5 per cent mortality and a 52 per cent five year survival.

This field of surgery demands a high degree of technical skill and seasoned judgment, and, if mortality figures are to be kept within reasonable limits, special training and experience are required. The establishment of a routine pre-operative preparation of the colon and physiological rehabilitation of the patient has in the past few years contributed greatly to the success of this type of surgery while meticulous postoperative care is essential. This routine, in which all those taking part in the care of these patients are carefully trained, has in my hands afforded the most gratifying results. Although the ultimate in perfection for the treatment of cancer of the rectum and rectosigmoid has by no means been reached, the vast strides which have been made during the past 25 years offer encouragement and inspiration for future advancement.

PECTIN IN THE TREATMENT OF VARIOUS TYPES OF WOUNDS

CHARLES A. TOMPKINS, M.D., GRACE W. CROOK, M.S., EDITH HAYNES, Ph.D., and MATTHEW WINTERS, M.D., Indianapolis, Indiana

EXPERIMENTAL work undertaken to explain the excellent results obtained by the use of the apple diet (8) and, later, a pectin agar preparation (3, 9, 10, 11) in diarrhea of infants, demonstrated that the pectin being used[1] had bactericidal action under certain conditions (2). Before subsequent work (1) showed that the bactericidal action which had been observed was due to nickel in the pectin first used, and not to pectin *per se*, we had speculated on the possible therapeutic action of pectin solutions in the treatment of infected wounds. Favorable response in the first cases led to further use of the material. Clinical evidence has accumulated to show that other pectins[2] as well as the nickel pectin mixture have definite value in the treatment of wounds.

METHOD

The pectin powder is used in aqueous solutions in percentages which vary according to the case to be treated. Solutions ranging from 2 per cent (on the basis of 100 grade pectin) to as high as a thick paste of 10 per cent have been used. The desired amount of pectin is weighed and mixed rapidly in cold water. For many of our cases the solution was sterilized in the autoclave for 20 minutes at 15 pounds pressure, but the addition of merthiolate makes sterilization by heat unnecessary and permits the use of a lower percentage of pectin, as heat reduces the viscosity. It was found that solutions of pectin may become contaminated with fungi, which grow in it since they are not so easily inhibited by the acidity of the solution (pH 3.4–3.8) as are most bacteria. To prevent this, aqueous merthiolate was added to make a dilution of 1:200,000. This not only prevented growth of fungi but added to the bactericidal effect of the solutions and yet was dilute enough that it was not toxic to tissue (6). Sterile gauze dressings are saturated with the pectin solution, or the solution is applied directly to the lesions as needed. The dressings are changed as often as necessary to keep them moist. Since this is an aqueous carbohydrate solution, excessive evaporation results in a tenacious stiff dressing which is difficult to change without tearing away new tissue. However, the pectin solutions give up the moisture slowly and by using vaseline gauze, oiled silk, heavy waxed paper or parafilm over the pectin dressings with a dry dressing over that, evaporation was reduced to a minimum. When used following sequestrectomies, the pectin dressings were changed two or three times a week; those of other types of wounds, usually at least once a day. Progress of the wound was followed by bedside notes, occasional bacteriological examinations and clinical photographs.

ANALYSIS OF STUDY

This report covers a period of three years beginning February, 1936, in which 75 patients were treated by this method of therapy with very satisfactory results. These were of the following general types: 25 decubitus and trophic ulcers; 23 chronic discharging wounds, such as osteomyelitis; 19 operative wounds with drainage or secondary infection; 5 superficial wound infections and 3 traumatic wounds. Fifty-seven of these were treated with the nickel pectin solution and 18 with nickel-free pectin solution. No essential difference could be observed in the results obtained in the two groups. The addition of the merthiolate (1:200,000) also caused no apparent difference in the results. Although only 8 cases were treated with pectin solution which did not contain merthiolate, it seemed impractical to omit it for a larger series of cases, because, as has been stated, it is necessary to add a preservative to prevent the growth of fungi in the solution.

Pectin dressings in the types of wounds treated bring about a prompt visible change in the wound. The wound takes on a healthy appearance and fills in from the bottom with rapid formation of granulation tissue. This new tissue is of a smooth bright red type with a healthy glistening sheen, is firm, and shows vigorous growth. The bactericidal effect of aqueous solutions of pectin, because

From the Departments of Pediatrics and Central Laboratories, Indiana University Medical Center. Aided by a grant from Mead Johnson and Company, Evansville, Indiana. Dr. Tompkins is now associated with the University of Nebraska College of Medicine, Omaha, Nebraska.

[1]Sardik Laboratories, Inc., New York City.

[2]Kindly furnished by General Foods Corporation, Battle Creek, Michigan.

Fig. 1. a, left, Appearance of lesion on February 11, 1936, 5 years after the accident. During these 5 years the wound had failed to heal sufficiently to justify attempting a skin graft. b, Showing successful skin graft on April 7, 1936.

of the high hydrogen-ion concentration (4, 5) and of the merthiolate and nickel, when present, appears to be only a part of the total therapeutic action. A considerable portion of the curative effect may be due to the hygroscopic property of pectin solutions which results in the decrease of edema in the granulations and leads to healthy wound healing. The granulation tissue thus formed, which is actively growing and apparently not edematous, seems to be able to rid itself of the effects of the infecting bacteria. The mechanical removal of organisms, pus, and serum, with change of dressings is probably also of some benefit. The acidity of the material does not seem to cause any irritation to tissue. Early in the course of treatment, the blood and pus in the wound decrease the acidity of the solution considerably, but at later stages of healing when very little body fluid is present, there is also no evidence of irritation. On the contrary, the application of pectin dressings to the various types of lesions decreases the discomfort according to statements of the patients, particularly in infected operative wounds. Another important feature is the absence of objectionable odors. This is especially noteworthy in cases of osteomyelitis, for the foul odors which are a very objectionable feature when some other methods of treatment are used, are not present in cases in which pectin solution is used. Their absence not only raises the morale of the patient, but also contributes to the satisfaction of the doctors, nurses, and others in the vicinity of the patient.

We do not feel that the pectin has any direct stimulating influence on epithelization; in fact, there are some indications that pectin inhibits that stage of healing. Accordingly, when a wound is clean and has filled to the desired degree, other medications are used to keep the lesion clean while the epithelial tissue grows. Much has appeared in foreign literature concerning the hemostatic action of pectin. However, we have been unable to observe positive clinical evidence to substantiate these claims for such marked local hemostatic action. Experimental work with animals in which we have used various pectin solutions to test for general and local hemostatic action following in-

Fig. 2. a, left, Lesion on October 6, 1936, at the time the pectin dressings were started. b, December 12, 1936 at time of discharge.

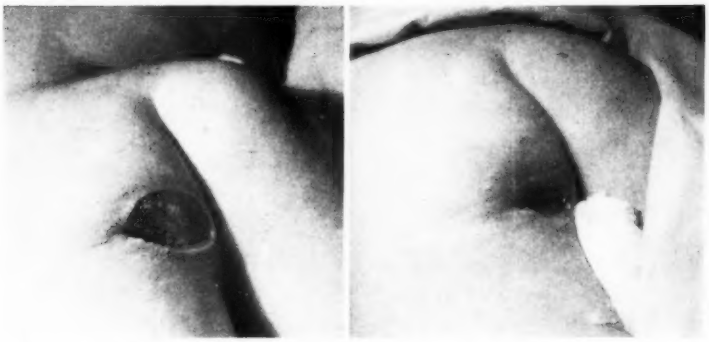


Fig. 3. a, left, Trophic ulcer on April 8, 1937. Area had become progressively larger for the past 2 years. b, May 3, 1937. Comparative photograph taken after 24 days of pectin treatment.

tramuscular and intravenous injections and local application gave evidence of some hemostatic action but of such a slight and transitory nature that its significance seems questionable.

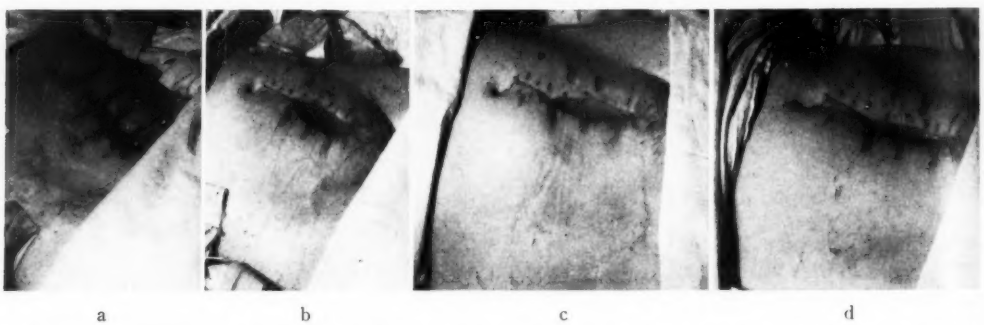
Except for the osteomyelitis cases we have no comparable series to serve as controls, as accurate records of the time required for the healing of wounds and ulcers treated by other methods were not available. However, controls for these types of lesions are practically impossible except in the broadest sense, for results depend on the entire treatment of the individual as well as on the local measures used, and the factor of case differences also does not permit definite comparisons. It can be stated, nevertheless, that with most of our patients the results exceeded the usual expectations and that in many instances wounds that had been treated by the customary measures with no success, showed prompt response to the pectin therapy. Results were good or excellent in practically every case. One superficial burn case and the one case of impetigo treated, failed to respond as did also a tuberculous nephrectomy wound in which sinuses continued to develop. In the osteomyelitis cases[1] healing time following sequestrectomies was reduced about one-fourth of that required under other methods of treatment which have been used here.

Thomson reports the use of 2 per cent pectin solutions in the treatment of old infected burns, pressure sores, infected soft tissue wounds, osteomyelitis, and infected compound fractures, and has confirmed the results obtained here.

CONCLUSION

After more than 3 years' use of pectin solution in the treatment of a sizable series of various types of wounds, we feel that such therapy results in a very prompt response with cleaner wounds and a rapid growth of highly vascular granulation tissue. The method seems to be of particular value

[1]These patients were under the supervision of Dr. George J. Garceau.



a b c d

Fig. 4. a, Appearance of abdominal wound July 9, 1938, before pectin dressings were started. b, July 25, 1938, after 15 days of pectin dressings. c, August 18, 1938; d, August 30, 1938, at time of discharge.

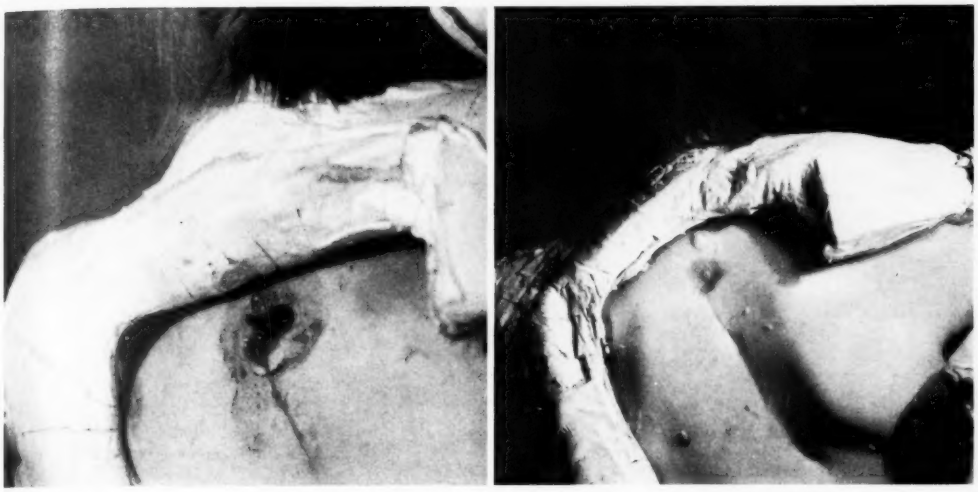


Fig. 5. a, left, April 25, 1938. Pressure sore on the back of a child, which developed following the second stage of a spinal fusion. b, May 23, 1938. Photograph taken at the time the child was furloughed. Back well healed.

in the chronic type of lesion which often resists all other therapeutic efforts and in those in which considerable growth of granulation tissue is required. This method of treatment is being continued in our hospitals with considerable satisfaction.

ILLUSTRATIVE CASE REPORTS

CASE 1. M. B., a white female, aged 15 years, admitted to the hospital February 17, 1936. Her physical examination was entirely negative except for an ulcerated lesion on the right foot (Fig. 1 a). The area was triangular in shape and involved a space 3 by 1½ inches on the medial and dorsal aspects of the foot. The foot had been injured in a train accident 5 years previous to this admission. During these intervening years she had been hospitalized at 2 different times for periods of 3 to 4 weeks. Therapy while in the hospital and at home had included chlorozene, scarlet red, merthiolate, and hot magnesium sulphate packs. Ultraviolet radiation and heat cradle had also been used. The lesion had failed to show any permanent improvement and the condition of the wound had never permitted attempting a skin graft. On this admission, treatment with 1 per cent chlorozene and elevation of the foot gave no apparent results. On February 20, 1936, a culture from the lesion of the foot showed hemolytic streptococcus and Staphylococcus epidermidis. Pectin dressings were started with a 2 per cent solution of nickel pectin with 1:5,000 merthiolate. This was the first wound treated with pectin solution and we were unaware of the presence of nickel in the substance. The merthiolate was added to be certain the solution was sterile. However, after the first application, we decided for experimental purposes to use 2 per cent aqueous pectin solution without merthiolate.

The wound promptly assumed a clean appearance and bacterial cultures showed a rapid disappearance of the streptococcus. Healing progressed at a most satisfactory rate. On February 29, 1936, the pectin was discontinued and chlorozene and ultraviolet were used in preparation for skin grafting. On March 13, 1936, three Thiersch skin grafts were applied. Following surgery the patient's condition was good, the grafts took well (Fig. 1 b) and she was discharged on April 9, 1936, with the wound healed. A check at a year and again at 2 years after the graft, revealed that the results were excellent.

CASE 2. J. C., white male, aged 4 years, was admitted to the hospital, September 23, 1936. Physical examination and history were essentially negative except for contused and lacerated tear on the left foot which had resulted from a street accident on September 22, 1936. Lesion had been closed with a primary suture at the time of the accident. At the time of admission some necrosis was believed present but it was thought best not to do a débridement. Antitetanus serum was given and continuous bath of ¼ per cent chlorozene was administered. The child's temperature was irregular up to 104 degrees F. The local discharge persisted and the general condition became alarming. The stitches were removed to permit adequate drainage and several of the metatarsal bones and their joints were found to be exposed (Fig. 2a). On October 6, 1936, dressings of 2 per cent nickel pectin solution without merthiolate were started. The discharge from the wound, from which Staphylococcus aureus and non hemolytic streptococcus were grown, decreased, and healthy granulation tissue proliferated at a very satisfactory rate. The temperature and general condition improved promptly and on October 22, 1936, the condition was satisfactory enough to transfer the child to the convalescent hospital where treatment was continued. On December 12, 1936, at time of discharge, the wound was healed except for a small area of granulation tissue on the dorsum of the foot (Fig. 2 b). The child had perfect motion of the foot, although an ankylosis of the involved joints had been expected.

CASE 3. J. E., white female, aged 10 years, was admitted to the hospital April 7, 1937. The child came in with the complaints of bilateral paralysis from the hips downward, incontinence, and ulcer on buttock. Spina bifida had been operated upon 13 hours after birth. The

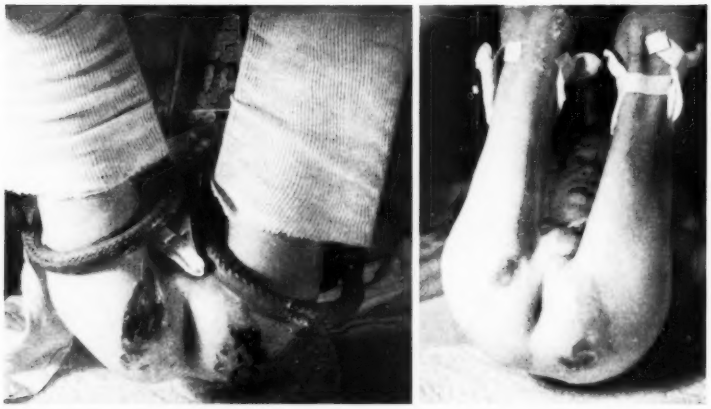


Fig. 6. a, left, July 20, 1938. Appearance of the pressure sores on the buttocks of Case 6 after pectin dressings had been used for 6 days. b, Marked progress noted on August 10, 1938.

child had been incontinent since birth and any injuries to the lower extremities had been very difficult to heal. Muscles of the lower extremities were atrophic, legs were small, and held in a flexed position. At this admission there was present a large ulcer on the medial side of the left buttock which had an indurated elevated margin and extended into the gluteal muscle. This ulcer, in spite of the use of various accepted treatments, had become progressively larger over a period of 2 years (Fig. 3 a). Cultures from the ulcer were found to contain Staphylococcus aureus, Escherichia coli, and an anaerobic gram-positive bacillus. Dressings of 3 per cent unautoclaved nickel pectin solution without merthiolate were used. Cultures taken 2 weeks after the treatment was started showed Staphylococcus aureus and non hemolytic streptococcus. The lesion responded with rapid appearance of healthy, firm granulation tissue forming from the bottom. Figure 3 b shows progress after 24 days of treatment when this child was released. Although the course of the pectin treatment was interrupted when the child went home, subsequent contact through out-patient clinics and the use of the pectin dressings at home resulted in a complete and permanent healing.

Case 4. M. W., white female, aged 19 years, was admitted to the hospital June 11, 1938. This woman had an abdominal hysterectomy, June 18, 1938, and 8 days later had to be taken to surgery again because of sudden evisceration through the abdominal wound during a coughing spell. An infection developed in the wound with a rapid breakdown to the peritoneum. The patient's condition was critical and the condition of the wound showed no improvement (Fig. 4 a). On July 9, 1938, treatment with 3 per cent autoclaved pectin without nickel but with 1:200,000 merthiolate was started. There was a prompt improvement in the appearance of the wound from which, on July 6, 1938, Streptococcus viridans, Escherichia coli and gram-positive bacilli were cultured. The pus decreased, the foul odor diminished, and the patient's temperature became normal. The comfort derived from these dressings was quite marked. Progress was very satisfactory as shown in the successive photographs (Fig. 4 b, c, and d). When she was discharged August 30, 1938, the wound was not completely closed but was healing in nicely. Out patient record showed the wound was well healed 4 weeks later.

Case 5. M. H., white female, aged 14 years, was admitted to the hospital January 5, 1938. This girl with paralytic scoliosis had developed a deep pressure sore down the margin of her cast and at the upper limit of her spinal fusion. This area was first noticed 5 days after the second stage of the spinal fusion had been done. The area was blackened, about the size of a quarter and involved a suture. It was treated with boric acid and alcohol and dry dressings for the next 12 days. The wound was opened, a penrose drain was inserted and a small amount of bloody, purulent drainage was released. The sore continued to drain and the interne reported that there was no improvement.

On April 25, 1938, when treatment with 4 per cent autoclaved nickel pectin solution with 1:200,000 merthiolate was started, the lesion was about the size of a silver dollar and full of pus (Fig. 5 a). Four days later the sore was reported better and much cleaner. Progress was most satisfactory and pectin was discontinued, May 18, 1938, before the granulation became exuberant. The back was well healed when the child was furloughed on May 23, 1938 (Fig. 5 b).

Case 6. D. S., white male, aged 8 years, was admitted to the hospital July 9, 1938. The boy was admitted suffering with fractures of both thighs and a compound fracture of the right ankle which had resulted from an accident occurring 6 days prior to admission. Very large and deep pressure sores on both buttocks were present at the time of admission.

Dressings of 3 per cent autoclaved pectin without nickel but with 1:200,000 merthiolate were started July 14, 1938. Figure 6 a shows the condition of the buttocks after 6 days of pectin treatment. Nine days later a definite improvement was recorded by the attending nurse. The subsequent progress of the sores was very rapid. August 10, 1938 (Fig. 6 b) the pectin treatment was discontinued.

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PRINCIPLES UNDERLYING TREATMENT OF SCOLIOSIS

By the Wedging Jacket

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ATTEMPT is not here made to outline the actual treatment of lateral curvature of the spine by the wedging jacket and spinal fusion. It does attempt to explain the theory of this method of treatment by assuming a simple dorsal curve and trying to explain the development and treatment of this curve. In preparing this paper, the author has made free use of the material offered in the fundamental articles by Ferguson and by Butte.

It is essential in studying the efficacy of any treatment of scoliosis that accurate records of the curve be kept from the time the patient first develops the curve or from the time of her first visit to the surgeon until the time occurs when there is no further increase in the curve.

The age period from about 6 to 11 years in girls, and to about 12 years in boys is a period when increase in height is not rapid. Untreated scoliotics in this age group may show no increase in the curve, or, if increase does occur, it is not rapid.

Rapid increase in height occurs in girls between the ages of about 11 and 15 years, and in boys between the ages of about 12 and 16 years. During this 4 year period, the progress of the curve in a scoliotic is the most rapid (Figs. 1 and 2).

From these facts it can be said that the effect of any treatment of scoliosis in preventing progress of a structural curve cannot be proved unless the patient is accurately followed up to and through this period of rapid growth. Thus, unless the treatment of a scoliotic begins before the age of 14 and unless accurate records of the curve are kept until this rapid growth period ceases, no evaluation can be made as to the efficacy of the chosen treatment.

The accurate method of measuring the progress of a curve is by repeated comparable roentgenograms taken at stated intervals. To do this a standing anteroposterior roentgenogram is taken of the entire spine from the first sacral vertebra up. The primary curve is considered to have an apex, the most rotated vertebra which is found at the crest of the curve, and an upper and lower end vertebra, the least rotated vertebra at either end of the curve. The centers of the shadows of each end vertebra and that of the apical vertebra are marked by dots. Lines are drawn from the apical dot to each end dot. This angle is measured. The angle of the curve is the difference between the angle formed by these two lines and 180 degrees.

From the above it can be seen that accurate check is possible in these cases. If a rapid increase in a curve occurs, this demands treatment. At our present state of knowledge, the only way to stop the progress of a curve is by spinal fusion of that curve. The sooner this is undertaken in a subject whose curve is increasing and who is not through the rapid growth period, the better the result will be. Exercises will not help these patients. Braces and jackets are useless (Figs. 1, 2, 3, and 4).

Operative treatment is indicated when a patient has: (1) a progressive curve which will lead to poor body balance and deformity; (2) a curve which is correctable, and, if corrected, will improve either the appearance of the individual, his health, or both; (3) a curve which is causing severe pain, and this can be relieved by spinal fusion.

If operation is to be undertaken, the spine should be corrected first, and this degree of correction maintained by spinal fusion. This correction is obtained by the wedging jacket.

To understand the principles of correction and the area to be fused, it is necessary to assume a simple, "S" type of curve and to follow this curve through its development, its correction, and the picking of the area to be fused. In this paper, we assume the development and the treatment of a right dorsal primary curve and the development of left cervical and left lumbar compensatory (secondary) curves.

In describing the development of the following curves, the fact that weak musculature is given as the cause of the curve developing is not to be construed as the true cause. This is chosen only as a method of explaining a deforming force. The cause of this deforming force is not known. It is not known whether this deforming force is in the form of a pull or a push, but the cause or nature of this deforming force is not important here. All that is needed is to realize that there is a deforming force attempting to bring one part of the spine closer to another part. And, further, if the spine is stabilized at the points where this force is acting, the movement of the spine by the deforming force is made impossible (Figs. 3 and 4).

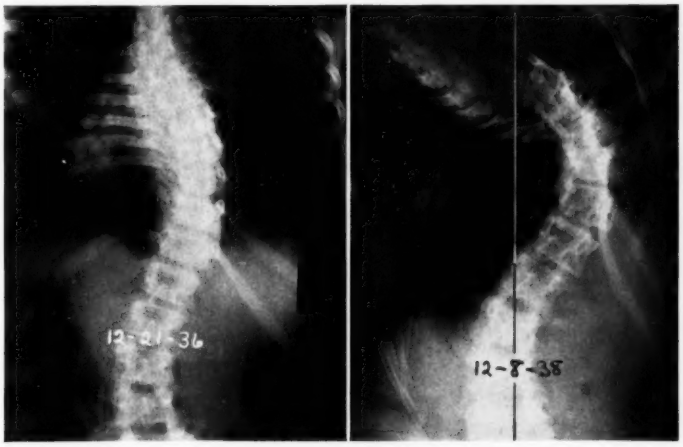


Fig. 1, left. At the time of this roentgenogram the patient was 11 years of age. The patient had been treated with exercises, braces, and jackets since she was 7 years of age at which time the curve was first noticed. Treatment up to 11 years had been considered satisfactory as the curve had not increased to any appreciable extent. The years from 11 to 14 will mark the rapid growth period for this girl. Primary curve from fourth dorsal to second lumbar; apex, tenth dorsal; neutral vertebra is second lumbar.

Fig. 2. Same girl as shown in Figure 1, 2 years later, at 13 years of age. In spite of continuous treatment by exercises, braces, and jackets the curve progressed rapidly between the years of 11 and 13. Notice the great increase in the right dorsal primary curve but comparatively little increase in the compensatory lumbar curve. Apparently the lumbar curve had reached its limit of compensation some time before this roentgenogram was taken. Since one cannot predict which patients will show marked increase in curvature during the rapid growth period, roentgenograms every 3 months are necessary in all cases until the rapid growth period is over. Right dorsal curve still from fourth dorsal to second lumbar; apex, tenth dorsal. Neutral vertebra is second lumbar.

The illustrations (Figs. 5 and 6) show the development of a primary right dorsal curve. To maintain body balance, compensatory curves have developed above and below the primary curve. These secondary curves are able to keep the head centered over the pelvis until their limit of compensation is reached. After this, any increase in the primary curve is not balanced by a reciprocal increase in the compensatory curves. Thus, body balance is upset, and a noticeable deformity results. Further, the compensatory curves are present only in response to the sense of balance. If the primary curve can be decreased in the wedging jacket to the extent that the compensatory curves can again bring the head over the center of the pelvis, and the primary curve is held in this position by spinal fusion, then, clinically, the patient will appear balanced (Figs. 3 and 4, 11 and 12). Or, if the primary curve is completely straightened and held straight by spinal fusion, no need for the compensatory curves exists. They will straighten and the spine, too, will be straight.

From the illustrations, it will be seen that a primary curve is one over which the patient has no control. A compensatory curve is one over which the patient can exert control and straighten at will, provided it is not present in response to a primary curve and must from necessity be present to maintain complete or partial body balance.

To distinguish a primary curve from a secondary curve, it is necessary to find the curves over which the patient has voluntary control and the curve over which the patient has no voluntary control. The curves the patient can control are compensatory curves. To fuse the compensatory curve with or without correction, instead of the progressing primary curve, would remove all compensatory tendencies from the spine. The unfused primary curve would still increase, and the resulting deformity would be more marked than if nothing had been done. Extreme in importance, then, is the picking of the true primary curve.

If it were possible to place the patient in such a position that to maintain her balance, she must

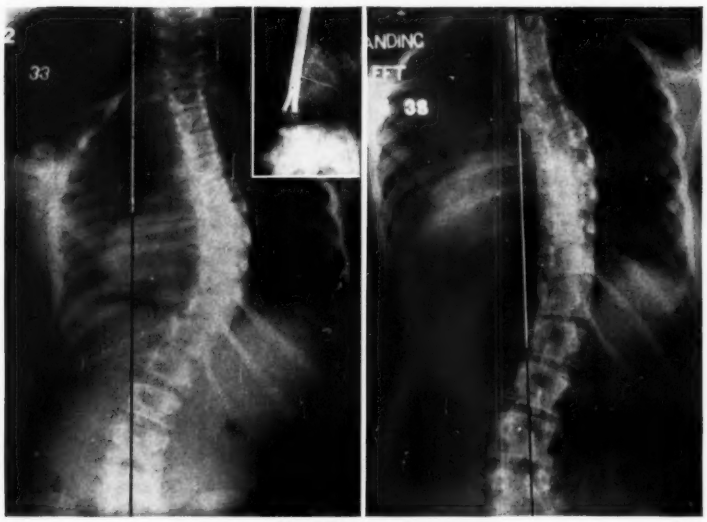


Fig. 3, left. This girl was 11 years of age when this roentgenogram was taken in 1933. The curve is more marked but in general it is comparable to the curve in Figure 1. Jacket correction and spine fusion performed in 1933.

Inset roentgenogram shows final (marker) roentgenogram. The wedging jacket has been fenestrated, the wire marker is over spine of the twelfth dorsal vertebra.

Fig. 4. Same patient as in Figure 3, 5 years after jacket correction and spinal fusion. The patient has maintained correction through her rapid growth period and appears clinically straight. Compare with Figure 3 and note that practically all correction has been maintained and that the compensatory curves now balance the primary curve thereby achieving good balance. Contrast with Figures 1 and 2. (Figures 3 and 4 by courtesy of the New York Orthopædic Dispensary and Hospital).

exert control over the curve in question, we could soon find out if she has control over that curve. If she has control over it, the curve is secondary. If she has no control over it, the curve is primary. This can be done. For this purpose the pelvic tilt roentgenogram is used (Fig. 7).

Pelvic tilt roentgenogram. These special views are taken primarily to test the muscle strength on the convex side of the lumbar curve. The patient sits on the edge of a table which is sufficiently high so as to prevent her feet resting on the floor. Her hands are in her lap giving no support to her trunk. The pelvis is now raised on the side of the convexity of the lumbar curve (the left side of the pelvis in Figure 7) by pushing flat objects, such as boards or books, under the left buttock. A point will be reached where the patient is tilted so far toward the right that a loss of body balance is threatened, and falling to the right is imminent. If the patient is now asked to straighten up from her position, she can do so only by straightening her lumbar curve. If she can straighten her lumbar curve, this curve is secondary. With the subject attempting to sit straight, an anteroposterior roentgenogram is taken of the spine from the first sacral vertebra up. Measurement of this lumbar

Fig. 5. This illustrates a normal child. The musculature is represented as equal on both sides of the trunk. The child through muscle tone and sense of balance is able to hold the spine erect. If the musculature were weak or absent in the right dorsal region the muscle pull as represented by the arrows would be more marked on the left side. Muscle imbalance would be present and a dorsal curve would develop with its convexity on the right side.

Fig. 6. This figure represents absent musculature on the right side of the trunk in the dorsal area. The dorsal curve is being pinched out at the weak point and a tendency for the trunk to go off balance is present. The primary right dorsal curve increases but through the patient's sense of balance the good musculature on both sides of the cervical and lumbar spine is stimulated to maintain balance by developing compensatory curves in the cervical and lumbar regions. The primary dorsal curve continues to increase rapidly. The compensatory curves cannot keep pace for this increase and the trunk shifts to the right. Thus the pelvis is unable to get under the center of the trunk and appears then to stay to the left, thus making the left hip prominent. This drawing illustrates compensatory curves that are past their limit of adequate compensation. Any increase now in the primary curve will result in complete

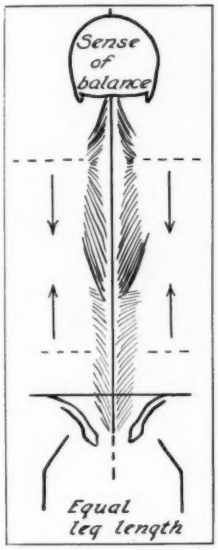
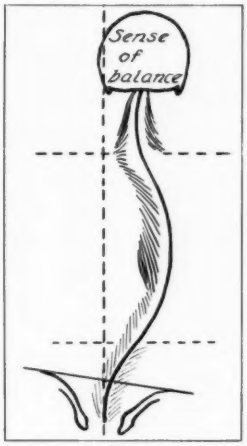


Fig. 5.



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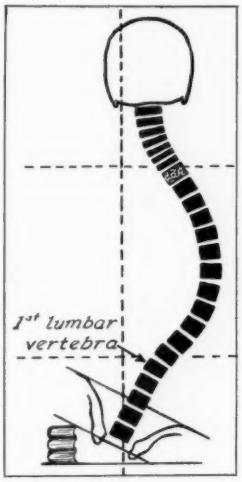

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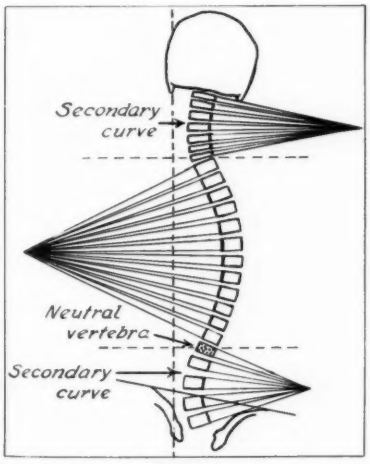
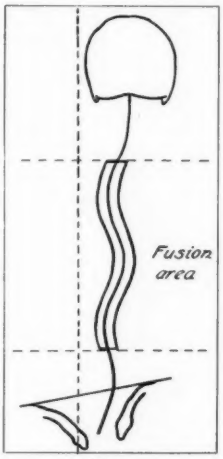


Fig. 8.



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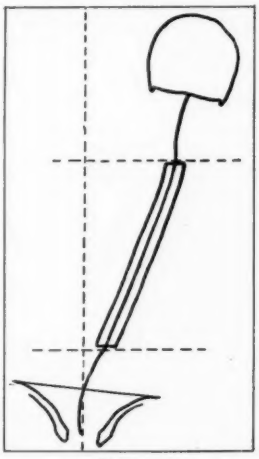

Fig. 10.

uncompensated deformity. (Compare with Figs. 1, 2, 3, and 4.)

Fig. 7. This left pelvic tilt plate represents the same curve as is shown in Figure 6. The primary right dorsal curve is shown as first dorsal to twelfth dorsal. The neutral vertebræ are the first dorsal and first lumbar. The tilting of the left pelvis has caused the lumbar spine to straighten completely. In this position the lumbar spine is the true axis of the trunk. All vertebræ below the first lumbar are straight and in line. The second lumbar vertebra in this case would be an ideal base for the solid column to rest upon. The ideal result in this case would then be obtained by wedging the dorsal spine completely straight if this can be done without overcorrecting the ends of the primary dorsal curve.

Fig. 8. Method of picking the extent of the different spinal curves. Note how lines change direction on each side of the neutral vertebræ. Same curve as shown in Figures 6 and 7.

Fig. 9. End-result of overcorrecting the ends of the primary right dorsal curve and then fusing them in an over corrected position.

Fig. 10. End-result of wedging the primary right dorsal curve straight and fusing the dorsal curve in this position when it has been shown by pelvic tilt that the lumbar spine is unable to straighten completely.

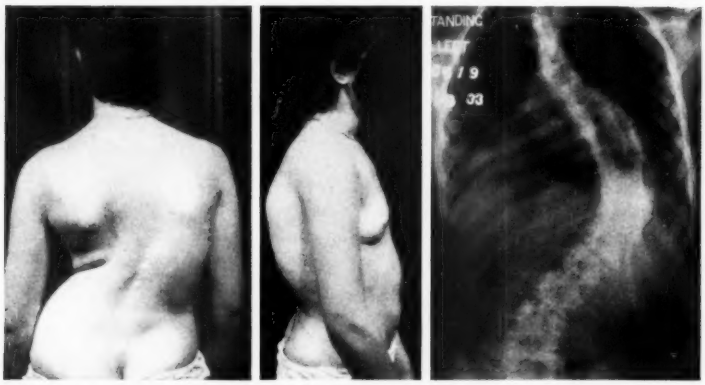

Fig. 11. Appearance of patient on admittance to New York Orthopædic Dispensary. Roentgenogram shows pseudo-arthroses. Fusion mass of inadequate length. Patient placed in wedging jacket and corrected through pseudo-arthroses. These repaired and fusion area extended to include third lumbar vertebra.

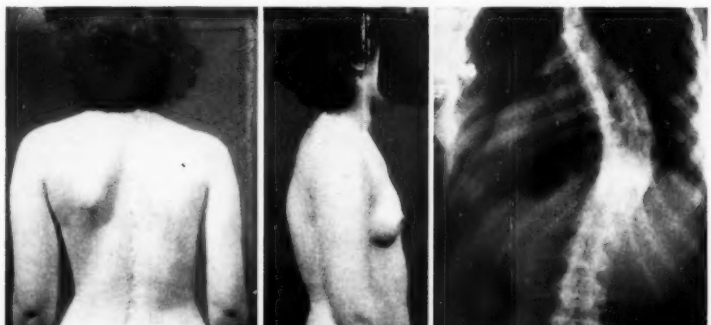

Fig. 12. The same patient 5 years after repair of pseudoarthroses and extension of the fusion area to include the third lumbar vertebra. Notice that a moderate primary right dorsal curve still exists but fair balance has been achieved. With this as a standard, the result obtained in the case shown in Figure 4 may be better visualized. (Courtesy of the New York Orthopædic Dispensary and Hospital.)

curve as compared with the lumbar curve in the standing view will give the answer to the problem (Figs. 7 and 8).

If, on the other hand, the right side of the pelvis is tilted in a similar manner, the left lumbar curve will increase. The right dorsal curve would then decrease in degree of curvature if it were secondary. Because of the immobilizing effect of the thoracic cage, a secondary curve in the thoracic region will not decrease as much as a secondary curve in the lumbar region when responding to the productive force.

If the right dorsal curve is primary, it will not decrease in degree of curvature with the right pelvis raised any more than a primary left lumbar curve will decrease in degree of curvature when the left side of the pelvis is elevated.

In conclusion then:

1. If the left lumbar curve is a compensatory curve, it will decrease in the degree of curvature when the left side of the pelvis is raised (Fig. 7).

2. If the left lumbar curve is primary it will not decrease in the degree of curvature when the left side of the pelvis is raised.

3. If the right dorsal curve is a compensatory curve, it will decrease in degree of curvature when the right side of the pelvis is raised, but not to the degree that a compensatory lumbar curve of similar degree would decrease.

4. If the right dorsal curve is primary, it will not decrease in the degree of curvature when the right side of the pelvis is raised. The patient is powerless to straighten a primary curve, whether it be dorsal or lumbar.

CLINICAL FINDINGS THAT AID IN DETERMINING THE PRIMARY CURVE IN THE SIMPLE "S" TYPE

1. The prominent hip is usually on the side opposite the convexity of the primary curve. If the hip findings and the pelvic tilt findings do not coincide with each other, detailed study of the patient to determine why not is essential.

2. The primary curve is usually the middle one of the three curves.

3. The primary curve is usually the greatest in degree of curvature because (a) the primary curve develops faster than the compensatory curves and (b) as far as is known, the compensatory curves never overcompensate for a primary curve.

If these statements are accepted, the following information has been gained:

1. The primary curve in the illustrations is considered to be the dorsal curve as it is taken to act as in Figures 6 and 7.

2. This primary dorsal curve has a deforming force working on it which is attempting to approximate one end of this curve to the other end. This must be stopped. To stop the effect of this deforming force on the primary curve, the whole area on which this deforming force is working must be fused.

3. To find this whole area, there must be a method of determining where the primary curve starts and where the primary curve ends—a method by which one can tell the extremes of the area on which the deforming force is working; that is, the upper and lower end vertebræ of the primary curve.

Choosing the extent of the primary curve. The primary curve has an apex, the most rotated vertebra in the crest of the curve. The primary curve has also an upper and lower end vertebra, and these end vertebræ mark the extent of the primary curve (Figs. 1 and 2). In looking at the standing roentgenogram of the spine (Figs. 1 and 2) the apical vertebra of the primary dorsal curve is located. As the eye travels from this apical vertebra to either end of the primary curve, it will be seen that the vertebræ of the primary curve become gradually less rotated and finally a vertebra is reached at each end of the curve which is not rotated. Beyond these unrotated vertebræ, the compensatory curves are beginning, and the vertebræ in the compensatory curves are rotated in the opposite direction than in the primary curve.

Further, the vertebræ in the primary right dorsal curve seem to be tilted so that the interspaces between the vertebræ appear more open on the right than on the left side of the vertebræ. If this tilt is followed from the middle both ways, it will be seen that this tilt becomes less marked as the ends of the primary curve are reached. At each end of the primary curve, there will be a vertebra in which the interspace is practically uniform in height between it and the vertebra next to it on the primary curve side. This vertebra is termed a neutral vertebra. If the eye follows along the spine away from this neutral vertebra in the direction of the compensatory curve, the vertebræ in the compensatory curve will be seen to tilt. But now the interspaces will be more open on the left instead of the right side. This neutral vertebra marks the end of the primary curve and the beginning of the compensatory curve (Figs. 1, 2, and 8). In this way the extent of the primary curve is found. The full extent of the primary curve is designated as the minimal fusion area.

AREA TO BE FUSED

Considering the area to be fused:

1. If, in an accurate pelvic tilt roentgenogram, it is seen that the compensatory lumbar curve has the power to return to the erect, this means that the primary curve can be straightened completely if possible. If the primary curve is wedged straight and is fused in this position, and the patient is released from all support after fusion is complete, the compensatory curves are able to bring the head over the center of the pelvis, and good to perfect balance is achieved. Thus, if the compensatory lumbar curve straightens completely on the pelvic tilt, one can give the primary curve all it will take in the way of straightening. In straightening a primary curve, it is important that it be brought only to the erect. It is very important that whether the apex of the primary curve straightens out completely or not, that the ends of the primary curve be not overcorrected. If the ends of the primary curve are overcorrected, and the curve fused in this position, the compensatory curves will have to be in the other direction, that is, reverse themselves, to compensate for this overcorrection. Body balance is again lost by this, but now in the opposite direction than before operation (Fig. 9).

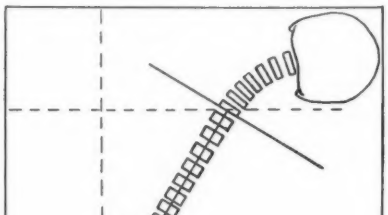

Fig. 13. Patient (Fig. 7) in wedging jacket after the dorsal spine has been completely straightened. Note that the lumbar spine is bent markedly in the direction of compensation. Also that the surfaces of the seventh cervical and the first lumbar vertebræ are practically parallel to each other and that a line joining the centers of these two vertebræ meet their transverse surfaces at a right angle. This illustrates the ideal. This figure represents final (marker) roentgenogram, since correction has been continued to the point where the best possible degree of body balance will be obtained.

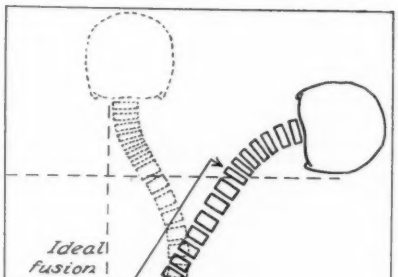

Fig. 14. Dotted figure represents pelvic tilt plate (Fig. 7). Note that the dotted lumbar vertebræ (pelvic tilt plate), are in direct line with the solid lined dorsal vertebra of the marker x-ray plate (Fig. 13). The composite spine (composed of the lumbar vertebræ of the pelvic tilt and the dorsal vertebræ of the final roentgenogram) is straight.

2. To achieve good body balance, it is essential that the primary curve and the compensatory curves work together. If, on pelvic tilt examination, the compensatory lumbar curve does not straighten completely, this will mean that the primary dorsal curve should not be straightened completely. The reason some compensatory curves have not the power to return to the erect is that they have been present for a long time and tend to become fixed, or the primary curve covers such a large extent of the spine that there is not enough of the compensatory curve to allow return to the erect. Control, however, is still active to a degree.

If the primary right dorsal curve were straightened out completely and fused in this position, in the face of a compensatory lumbar curve that had been shown to be unable to straighten completely, the patient would be unable to bring the trunk completely back to the erect and, consequently, would be left with a list toward the right (Fig. 10).

A mean, therefore, must be established in which the compensatory curves balance the primary curve. Thus, the whole will be a straight line between the center of the head and the center of the pelvis, regardless of the spinal curves in between (Figs. 1 to 4, 11, and 12).

3. In each vertebral joint there is so much motion. Decompensation occurs when the compensatory curves reach the degree of curvature that utilizes the movement inherent in the vertebral joints making up the compensatory curves. The compensatory curves then can go no farther in the way of compensation. Any increase in the primary curve beyond the limit of secondary curve compensation will lead to an uncompensated deformity which is permanent unless treated (Fig. 6).

If, then, a compensatory curve is shown by pelvic tilt examination to be able to straighten completely, what mistake at operation could be made to prevent the complete straightening of this compensatory curve? The mistake would be to fuse into the compensatory curve to such an extent that in the vertebral joints of the compensatory curve spared at fusion there would not be enough motion left to enable the spine to return to the erect. In other words, the fusion area would be too long. This might occur at either end of the primary curve.

4. If the area fused at operation is too short, all of the primary curve will not be included in the fusion mass. When all support is removed, the compensatory curves which are capable of balancing the patient are forced to compensate for the area of the primary curve not in the fusion mass. The patient will develop the same deformity as before operation, only to a lesser degree. If the primary curve increases in the unfused portion of the spine, this decompensation may be-

come marked. This is why the *entire primary curve* is termed the minimal fusion area.

5. Fusing one vertebra too long or one vertebra too short in certain cases may be enough to cause failure in balance. The advantage of having an accurate method of telling the operator which vertebra he is starting with is important. This is the purpose of the marker roentgenogram (Fig. 3).

The ideal fusion area. This is that area of the spine chosen for fusion after sufficient correction of the primary curve has been produced to restore the patient to the best possible degree of body balance. This area can be chosen only after correction of the curve has been completed in the wedging jacket. After wedging is completed, the area of the compensatory curves adjacent to the end of the primary curve are bent in the direction of compensation. The ideal fusion area must go slightly beyond the extent of the primary curve and into these adjacent areas of the compensatory curves. The reasons for this are:

1. That wedging is continued until, in the area of the compensatory curve immediately above the primary curve, and in the area of the compensatory curve immediately below the primary curve, there will be finally one vertebra in the area above the primary curve whose transverse surface is approximately parallel to the transverse surface of one vertebra in the area of the compensatory curve just below the end of the primary curve. These transverse surfaces should not only be parallel with each other, but these two vertebræ should be in such alinement that a line joining their centers will pass through their transverse surfaces at approximately a right angle. If the two vertebræ showing this relationship are included in the fusion mass, then the top vertebra in the fusion mass will be directly over the lower vertebra in the fusion mass. A straight line between the two ends of the fusion mass is thus obtained regardless of the curves in between. Thus, the fusion mass will include a portion of each of the compensatory curves which by fusion will be permanently fixed in compensation. The rest of the compensatory curves then will have less to compensate for and will become more straight and flexible (Figs. 3, 4, 11, 12, 13).

2. If this relationship is achieved, a base must be found for this solid column of bone to rest on. The transverse axis of this base obviously must be at right angles to the vertical axis of the column, since the column will, of necessity, take the direction of the base it rests upon. If the base is not level, the column will list.

The only roentgenogram that gives any clue to the ultimate base for this column to rest upon is

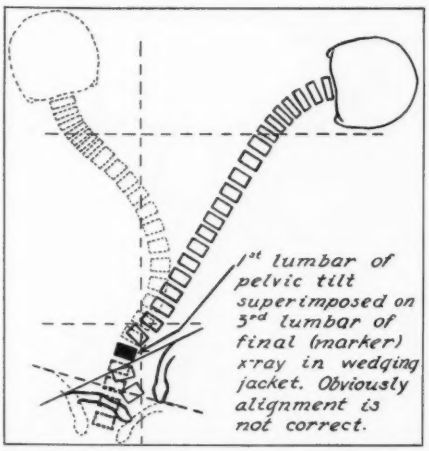
1st lumbar of pelvic tilt superimposed on 3rd lumbar of final (marker) x-ray in wedging jacket. Obviously alignment is not correct.

Fig. 15. Figures the same as in Figure 14. Note that the lumbar spine of the pelvic tilt plate does not line up with the dorsal spine of final (marker) roentgenogram. If spine were fused to include the third lumbar vertebra the area would be too long.

the pelvic tilt plate. In the *ideal* case, as illustrated in the drawings, the pelvic tilt drawing (Fig. 7) shows straightening of the lumbar spine. In Figure 7, it is seen that the first lumbar vertebra and all vertebræ below it have their transverse axes practically at right angles to the lower portion of the trunk, and a line dropped from the center of the first lumbar vertebra will pass through the center of the sacrum. This, then, represents the true axis of the trunk. Further, this pelvic tilt drawing indicates that there is enough motion in the joints of the vertebræ below the first lumbar vertebra to allow return of the lumbar spine to the erect if it did not have to compensate for the primary dorsal curve.

Naturally, in the wedging jacket, the lumbar spine will be bent markedly in the direction of compensation (Fig. 13). But, in the case illustrated, the first lumbar vertebra has lined up with the seventh cervical vertebra in the ideal manner (Fig. 13). Since the pelvic tilt roentgenogram of this case (Fig. 7) has shown that the lumbar spine can return to the erect, the ideal fusion area is easily visualized as the seventh cervical to the first lumbar vertebræ.

After correction is obtained in the wedging jacket, the cervical and the lumbar spine will be bent markedly in the direction of compensation (Fig. 13). If one should fuse too far into this area the lumbar spine would be permanently fixed in marked compensation. After release from sup-

port there would then be a list of the trunk to the right. Before operation the left hip was prominent (Fig. 6) but after operation the right hip would be prominent. The fusion area would be too long.

The question now arises: How can one visualize the end-result, and thus select the ideal fusion area in cases in which complete straightening of the primary curve does not occur? This is done by superimposing the final (marker) roentgenogram in such a way that the end vertebra of the proposed column, as shown in the marker roentgenogram, rests on its proposed base as shown in the pelvic tilt plate (Fig. 14). If faulty selection has occurred, superimposition will show the error (Fig. 15). Correctly done, this procedure will obviate the mistake of fusing too long or too short an area.

The final fusion area can then be visualized only after the wedging is completed. It is, in effect, matching the degree of straightening of the compensatory lumbar curve, as shown by the pelvic tilt roentgenogram, with the degree of straightening of the primary curve as obtained in the wedging jacket.

Obviously, after alinement is obtained, any loss or increase of correction would alter the extent of the fusion area and the degree of balance. This is why the jacket is fenestrated, and all operations are carried out while the patient is in the wedging jacket. To avoid loss of correction after operation, the patient is kept in the wedging jacket for a period of at least 3 months before the semi-bent jacket is applied, and the patient allowed up.

Pseudo-arthrosis. In one group of surgeons experienced in this operation, pseudo-arthrosis occurs in about 10 per cent of the cases operated upon. The failure of one vertebral joint to fuse in the primary curve is enough to allow loss of correction sufficient to cause a loss of body balance. When a pseudo-arthrosis occurs, the curve increases, and the patient retrogresses toward the decompensation present previous to operation. If a pseudo-arthrosis is present and is found only after body balance is lost, jacket correction through the site of pseudo-arthrosis is done, and then the defect is repaired (Figs. 11 and 12).

The presence of pseudo-arthrosis should be suspected: (1) when there is pain and tenderness in the fused area of the spine; (2) when there is quite pronounced loss of sitting height; (3) when a definite line of defect in the fusion mass is shown by roentgenogram; (4) when the roentgenogram shows an abnormal tilt of one or more of the vertebræ in the fusion mass as compared to the position of these vertebræ as shown in the roentgenogram taken previously of fusion mass; (5) when there is a steady, marked increase of curvature in the primary curve, either while patient is in the body jackets or after release from all support.

Normally, there is a settling of the solid fusion mass the first year after operation which allows some increase in the primary curve. The amount of this increase is not definite. In general, a loss of 15 degrees in moderate curves is to be expected. The more marked the curve, the greater the degree of settling. This settling must be allowed for when estimating the extent of the area to be fused.

If a pseudo-arthrosis is suspected, the spine should be explored before loss of correction is marked, and the defect repaired.

CONCLUSIONS

1. The majority of scoliotics, with or without conservative treatment, do not develop a marked degree of curvature.

2. Since one cannot predict which child will develop a marked degree of curvature, all patients should have comparable roentgenograms taken of the spine every 3 months until the danger of further increase in curvature is past.

3. The great increase in the primary curve occurs during the rapid growth period.

4. If a curve is shown to be increasing, the sooner the patient is corrected and fused, the better the result will be. One should not wait until the rapid growth period is over to begin operative treatment, but should begin the treatment as soon as it is indicated. In this way, the amount of correction to be gained is less, the spine is more flexible, the distortion of the thoracic cage is not as marked and the result is far better.

5. At the present state of knowledge of this condition, early correction of the progressing curve by the wedging jacket and the maintenance of this correction by spinal fusion seems to be the method of choice. It is the only method that will prevent the marked deformity that occurs in a certain percentage of children afflicted by scoliosis.

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THE TREATMENT OF FISTULA AND OBSTRUCTION OF THE SMALL INTESTINE BY COMPLETE EXCLUSION

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THE operation of complete exclusion offers certain advantages in the treatment of fistula and of obstruction of the small intestine. Although not new, the operation is generally unfamiliar. Its advantages for fistula are: first, the restoration of the continuity of the intestinal tract by an anastomosis around the fistulous segment of intestine. Second, the complete exclusion of the fistulous segment, which may be excised then or later as desired. Third, the performance of the operation in a clean field well away from the fistula. Fourth, the fact that the operation is well tolerated even by debilitated individuals. The operation recently was performed on 3 patients with fistula of the ileum, and proved a life-saving measure after other standard procedures had failed.

The exclusion operation is of further value in acute obstruction with gangrene of the small intestine, because it effectively controls fistula following exteriorization of nonviable intestine. This is illustrated by the treatment of the first and second patients of this series. Both patients had gangrene of the ileum, both were debilitated, and neither would have tolerated resection of the gangrenous ileum with anastomosis at the original operation for acute obstruction. Exteriorization was performed; yet the fistula which resulted resisted all attempts at closure by stages 3 and 4 of the Mikulicz operation, and persisted despite attempts at closure by mechanical methods. At a time when the patients were failing rapidly, the exclusion operation was executed. Both patients made a rapid recovery.

The exclusion operation is applicable to any type of fistula of the small intestine. It was successfully performed on the third patient of this series for fistula due to terminal ileitis. Indeed, intestinal exclusion was originally devised to treat adhesions or tumors, but its use for fistula is relatively recent.

LITERATURE

Trendelenburg, in 1885, and von Hacker, in 1888, first described the principle of intestinal exclusion. Salzer, in 1891, used it for lesions of the cecum, and a modification of his procedure is familiar today in the form of end-to-side ileocolostomy with partial exclusion of the cecum. The Devine operation for inoperable carcinoma of the stomach represents another type of partial intestinal exclusion.

To control fistulas of the small intestine, Cokkinis and Ginzburg employed the operation of complete exclusion. Cokkinis, in 1936, reported a patient with strangulated femoral hernia and gangrene of the ileum. He resected the ileum by a Mikulicz exteriorization procedure. To close the resulting fistula he performed the complete exclusion operation and after 11 months excised the blind fistulous segment of intestine. Ginzburg, in 1940, reported the use of the complete exclusion operation in 6 patients with fecal fistulas due to terminal ileitis.

OPERATIVE PRINCIPLES AND TECHNIQUE

The purpose of the complete exclusion operation is to restore the continuity of the intestine, and to remove completely the intestinal current from the fistulous segment of intestine. The operation is therefore called complete exclusion, and is sometimes also referred to as bilateral exclusion. It must be distinguished carefully from the operation of partial or unilateral exclusion, in which the fecal current is only partially diverted from the fistulous segment. This distinction is important; and failure to appreciate it has, at times, led to failure to close a fistula. Hereafter, when the term "exclusion" or "exclusion operation" is used alone, it refers only to complete exclusion, and not to partial exclusion.

The steps in the operation of complete exclusion are as follows. The incision is made well away from the fistula, through fresh skin, and ordinarily through the left rectus muscle. The peritoneum is thereby incised at a distance from those adhesions or abscesses which may surround the fistula.

Catheters are now inserted by an assistant through the fistula, one into the proximal and one into the distal loop of intestine. The surgeon next identifies both these loops within the abdomen, and severs each between clamps (Fig. 1). He in-

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verts the two ends which lead to the fistulous segment of intestine, and replaces them within the abdomen. He anastomoses the two remaining ends, the side-to-side technique being here employed. The abdomen is closed without drainage.

Following operation, the fecal current again flows entirely within normal channels, and none reaches the fistulous segment. The latter becomes a blind pocket of intestine without digestive function, and secretes small quantities of non-irritating chyme. It functions as an effective plug against herniation, being anchored posteriorly by the mesentery, and anteriorly by the fistulous tract itself. In this form it may be left indefinitely or removed at a later operation.

CASE REPORTS

CASE 1. Mrs. A. A., housewife, aged 71 years, was seen by courtesy of Dr. Walter Fischel. She was admitted to St. Luke's Hospital (No. 22448) on March 6, 1939, with acute intestinal obstruction of 22 hours' duration. The obstruction was due to strangulation of a postoperative ventral hernia. Laparotomy for acute appendicitis had been performed in 1929 through a right rectus incision, and a hernia resulted which had periodically become strangulated during the 10 years 1929 to 1939, but had never previously been irreducible. Exploration revealed about one-third of a meter of high ileum to be gangrenous. Due to the poor condition of the patient an obstructive resection was done. The gangrenous intestine was exteriorized and resected between clamps, and the two loops were left side by side on the abdomen. The wound was closed to the loops, but the hernia was not repaired. The clamps were removed the next day, and the spur was crushed on the third day. The wound healed as far as the stoma. There was severe skin excoriation and a large portion of the intestinal secretion was lost through the fistula. Mechanical measures, such as buttons and tubes, failed to return the fecal current to the normal channel. On the eighth postoperative day an attempt was made to close the fistula by the fourth stage of the Mikulicz procedure, under local anesthesia. The two loops of intestine were dissected away from the skin and subcutaneous tissue down to the peritoneum, and were anastomosed. The skin was closed over them. However, the fistula recurred 2 days later and the patient failed, this time more rapidly than before. On March 28, 1939, the exclusion operation was performed (E.L.K.) under ether anesthesia as illustrated in Figure 1. Note that the anastomosis was near the site of a Meckel's diverticulum. There was immediate and rapid improvement. Aside from an infection of the left parotid gland, there were no complications and the patient was discharged May 1, 1939. She resumed work shortly thereafter and has been performing household duties during the subsequent 14 months. The blind fistula (Fig. 2) discharges mucus which does not irritate the skin and which necessitates light dressings three or four times daily. A surgical support is worn. The hernia is effectively plugged by the blind loops and there has been no further strangulation. The patient refuses resection of the blind loops.

The fistula which developed in the mid-ileum of a woman of 71 after obstructive resection of gangrenous ileum strangulated in a postoperative ventral hernia could not be closed by stages 3 and 4 of the Mikulicz procedure or by mechanical measures. The operation of complete exclusion was successful. The patient has worked for over a year since. The hernia is plugged by the blind loops of the excluded intestine (Figs. 1 and 2).

CASE 2. Dr. A. M., a Rabbi, aged 71 years, was seen by courtesy of Dr. Alfred Fleishman. The patient was admitted to the Jewish Hospital (No. 109297) on February 17, 1940, with an acute intestinal obstruction of 18 hours' duration. Exploration revealed 2 meters of gangrenous mid-ileum which had herniated through a defect in the mesentery of another loop and in so doing had strangulated its own mesentery. An obstructive resection was done immediately, with exteriorization of the diseased intestine; the proximal and distal loops being brought out together and clamps left applied. Anastomosis was not done because of the patient's precarious condition. On the third postoperative day, the clamps were removed from both loops and a double-barrel ileostomy resulted. The wound healed by primary union. On the seventh postoperative day the spur was crushed. Large amounts of intestinal juices were lost through the fistula and the patient rapidly became worse. The crushing of the spur did not help to return the fecal stream to normal channels. Catheters and curved glass tubes also proved unsuccessful in shunting the drainage from the proximal into the distal loop. On the twentieth postoperative day, under spinal anesthesia, the fistula was closed by mobilization and end-to-end anastomosis. The anastomosis was not replaced within the abdomen but was left extraperitoneal beneath the skin. The fistula recurred and the patient's condition became critical. It was decided to do the exclusion operation. For the 2 days prior to this, a Miller-Abbott tube was inserted into the distal loop for feeding purposes, and to prevent regurgitation from this loop. This maneuver helped no little in preparing the patient. On March 20, 1940, under local and cyclopropane anesthesia, the exclusion operation (Fig. 3) was performed (I.C.M.). The patient made an excellent recovery, and the wound healed well. The patient was readmitted after 10 weeks, and the blind loops, measuring 25 and 30 centimeters respectively (Fig. 4), were resected, under general anesthesia. The defect in the abdominal wall was repaired as for a postoperative hernia. Recovery was uneventful, and the patient has since resumed his duties.

A fistula developed high in the ileum of a man of 71 after obstructive resection of a gangrenous segment strangulated in a defect in the mesentery. The operation of complete exclusion was successful after other measures had failed. Ten weeks later the blind loops were successfully resected.

CASE 3. Mr. J. H., an accountant, aged 45 years, developed regional enteritis of the jejunum about 1927. Medical treatment proved unsatisfactory. Surgery, in 1931, consisted in entero-enterostomy about the diseased jejunum, and in 1937 the diseased jejunum was resected. Following temporary improvement, enteritis flared up in the terminal ileum. Surgery in 1939 consisted in a two-stage resection of the terminal ileum and of the right half of the colon. A fistula appeared for the first time subsequent to the second stage, on July 27, 1939. The fistula originated from the inverted end of the ileum, and ran along a posterior stab wound to terminate in the right flank. The fistula persisted despite local measures, and laparotomy for cure was performed on December 30, 1939. Through a right subcostal incision, the tract was excised after it was traced to its origin in

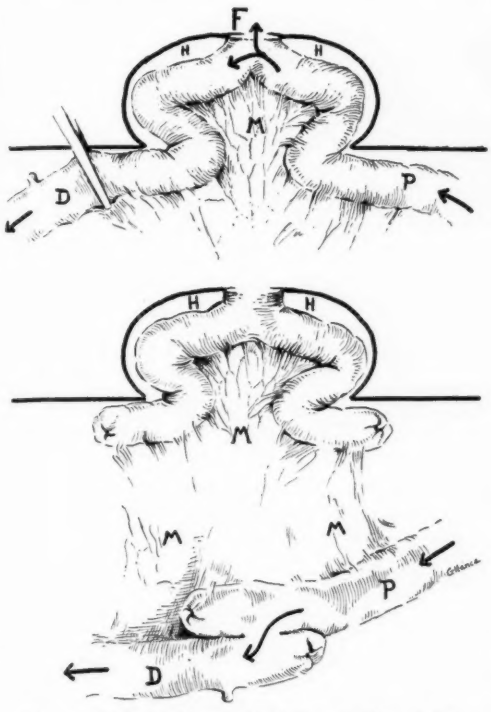


Fig. 1. The complete exclusion operation, Case 1. A, above, uncontrollable fistula following exteriorization of gangrenous ileum. B, below, operation ended, fistula completely excluded. *F*, Fistula; *H*, hernia; *M*, mesentery; *P*, proximal loop; *D*, distal loop. A Meckel's diverticulum is indicated.

the terminal ileum beyond the anastomosis. The ileum and colon in this region were dissected free in an effort to find intestine suitable for re-anastomosis, but the ileitis, scar tissue, and burrowing abscesses were too extensive; and the operation was concluded by marsupialization of the open end of ileum. A huge fistula of the ileum at its junction with the transverse colon resulted (Fig. 5). The fistula was successfully plugged with sponge rubber for 2 months, but the ileum then became too irritable any longer to tolerate the plug. Almost the entire fecal stream was lost and the patient's condition became bad. In view of its success in Case 1, the exclusion operation was again chosen, and was performed (E.L.K.) on April 1, 1940 (Fig. 5). Convalescence was rapid, and the patient was discharged on the nineteenth postoperative day. He gained weight and has worked steadily since May 20, 1940.

A fistula developed in the high ileum of a man of 45 as a result of operations for regional ileitis. Failure followed attempts to close the fistula by operation, and the situation became critical. The operation of complete exclusion proved successful. The patient resumed work 1 month later.

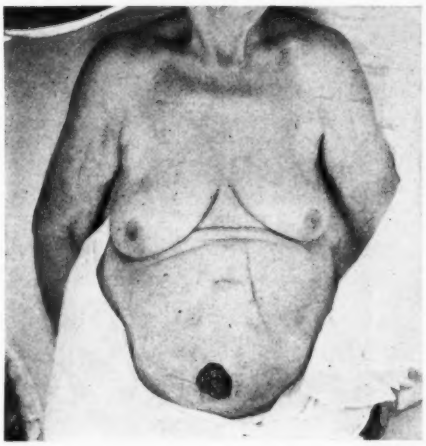


Fig. 2. View of first patient to show hernia plugged by the blind fistula following its complete exclusion by operation. This figure corresponds to Figure 1B. The left rectus scar results from the complete exclusion operation.

ADVANTAGES OF COMPLETE EXCLUSION

The operation of complete exclusion proved successful in treating three debilitated individuals with persistent fistula high in the ileum. By this operation, and after failure of other methods, the continuity of the intestinal tract was restored at a critical time.

The complete exclusion operation offers a means of overcoming certain difficulties sometimes insurmountable by the three standard surgical procedures for treating fistula. The salient points will be discussed as they relate to the three operations, namely (1) exteriorization of the Mikulicz type; (2) the one-stage operation of excision of the fistulous tract, resection of the fistulous segment of intestine, and immediate anastomosis; (3) the operation of partial exclusion, including (a) side-to-side and (b) end-to-side anastomosis around the fistula.

1. *Exteriorization of the Mikulicz type.* Gangrenous small intestine causing acute obstruction is frequently exteriorized because this operation is less dangerous than primary resection with anastomosis. The plan then is to close the resulting fistula by crushing the spur and later by anastomosis. Fistulas of the small intestine, however, can rarely be closed by such simple steps; and many deaths occur due to fistulas persisting despite these maneuvers. It was the plan in Cases 1 and 2 of this series to close the fistulas by these stages of the Mikulicz operation, but the fistulas would not remain closed. Neither patient

would probably have survived the extensive operation of resection of the fistulous segment of intestine with primary anastomosis. In this difficult situation, death was narrowly averted by the use of the operation of complete exclusion.

From this experience of successfully controlling fistulas following exteriorization, it is hoped that exteriorization for gangrene of small intestine may be more widely used in the future. In the past, exteriorization has often been avoided by surgeons because of the extreme difficulty of successfully dealing with the fistula of the small intestine which necessarily follows exteriorization. To avoid fistula of the small intestine, surgeons often attempt unwisely to resect gangrenous small intestine which causes acute intestinal obstruction and to perform primary anastomosis; an operation which carries a very high mortality, often over 50 per cent. With the realization that fistula of the small intestine can be successfully controlled by the operation of complete exclusion, the method of treating acute intestinal obstruction which requires resection of the small intestine may undergo change, and the high mortality of this distressing condition may be lowered.

These remarks, of course, do not apply to the treatment of obstruction of the large intestine, for in such cases the Mikulicz measures are of unquestioned merit.

2. The one-stage operation of excision of the fistulous tract, resection of the fistulous segment of intestine, and immediate anastomosis. Any extensive operation would probably not have been tolerated by the 3 patients of this series. The one-stage operation of excising the fistulous tract, resecting the fistulous segment of intestine and anastomosis might well have proved fatal. On the other hand, the operation of complete exclusion proved safe and was tolerated surprisingly well by these debilitated individuals.

The complete exclusion operation serves actually to break an extensive one-stage procedure into two stages, the first stage being the exclusion operation itself, and the second stage being the resection of the blind fistula.

The complete exclusion operation when used to treat fistula attacks the important part first. The anastomosis is performed before the fistulous loop of intestine is resected. The blind loops which lead to the fistula may be dealt with immediately or later as the condition of the patient indicates. This is in contrast with the usual method of dealing with a fistula of the small intestine, in which the incision is usually made down along the fistulous tract, the fistula dissected out, the connecting intestine identified by a tedious dissection and finally cut away, leaving the anastomosis to the last part of the operation. The usual operation proceeds from a dirty field to a clean field whereas the complete exclusion operation begins in a clean field and ends there.

The second stage of such a procedure as this, namely, the resection of the blind loops, is optional. Thus the first patient refused resection of the blind loops and lived reasonably comfortably for over a year, doing her household duties. These blind loops effectively plug the postoperative hernia which was the original cause of strangulation. For the 14 months since the exclusion operation this patient has been free from strangulation; previously, she had suffered periodical strangulation. The second patient, on the other hand, was carried through the second-stage operation 10 weeks after the exclusion procedure. The blind loops were resected and the hernia through which they protruded closed. Had these two stages been done as one it is doubtful that he could have survived. The third patient has returned to work without resection of the blind loops. He has already undergone six major operations for regional enteritis.

Similar two-stage procedures were employed by Cokkinis and by Ginzburg. Cokkinis performed an exteriorization operation for acute obstruction due to strangulated femoral hernia with gangrene of the ileum; being unable to close the resulting fistula, he successfully performed the complete exclusion operation. Ten weeks later he resected the blind loops.

Ginzburg also used the operation of complete exclusion for treating 6 patients with fecal fistula due to terminal ileitis. He later resected the blind loops in some of these cases.

An interesting use of the exclusion operation is illustrated by a patient of Dr. Nathan Womack's. This patient developed a fistula of the ileum following exteriorization of gangrenous intestine. Dr. Womack, being familiar with the operation of complete exclusion, performed a left rectus incision with the idea of utilizing the operation. After he had done the anastomosis and excluded the fistulous segment, the patient's condition was so good that he proceeded at once to resect the fistulous loops without waiting to do so at a second stage. The patient made an uneventful recovery.

This mode of using the complete exclusion procedure seems worthy of wide application. It would seem safer, less unsterile, quicker, and more flexible than the usual procedure for reasons enumerated several paragraphs above. The operation goes from a clean to a dirty field, the anastomosis

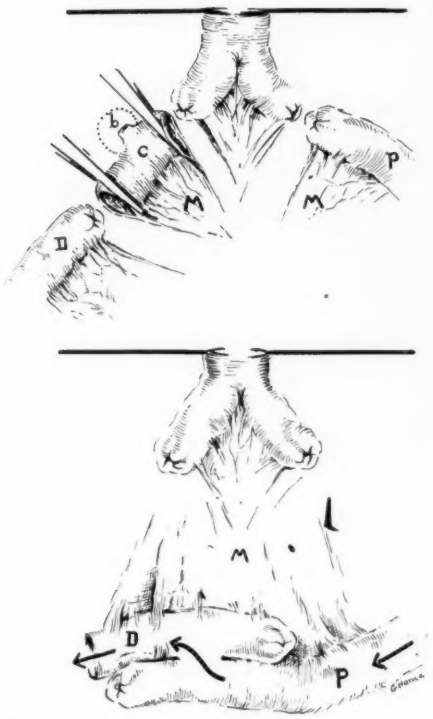


Fig. 3. The complete exclusion operation, Case 2. A, above, uncontrollable fistula following exteriorization of gangrenous ileum. Operation begun by resecting segment *C* because of perforation *b*. B, below, operation completed, fistula entirely excluded. *P*, proximal and *D*, distal loops; *M*, mesentery.

is done at the outset, and the operator can stop there if he desires. The operation begins with the easy and the important part, namely, the anastomosis. The tedious, relatively unimportant, and often unsterile part of dissecting the fistulous tract down to the intestine and mobilizing the intestine is left to the end of the operation, or to a second stage if so desired.

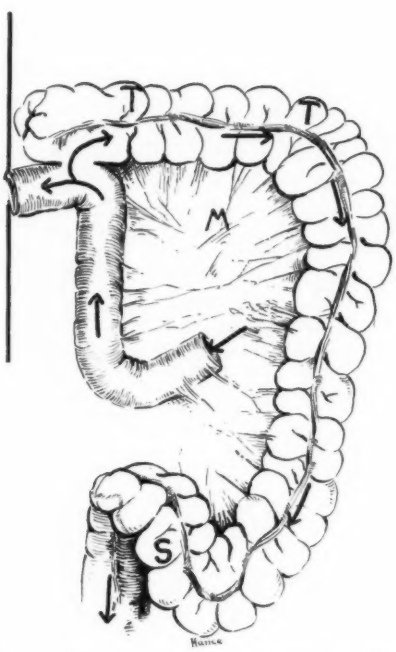
3. Operations of the partial type of exclusion. Near the beginning of this article, the reader was asked carefully to distinguish between complete exclusion and partial exclusion. Partial exclusion, as for instance end-to-side ileocolostomy, is sometimes recommended to treat fistula. It is to be condemned, because the intestinal contents continue to find their way through the fistula, and because spill-over may occur into the blind loop. This loop may distend and cause new symptoms, necessitating its resection or complete exclusion.

Fig. 4. Barium has been introduced through catheters into the two blind loops following their complete exclusion by operation. This figure corresponds to Figure 3B.

Cokkinis recommends a side-to-side anastomosis as a step in the operation of exteriorization of the small intestine for acute obstruction with gangrene. This step he argues will help in closing the subsequent fistula. If side-to-side anastomosis has been performed at the time such exteriorization was carried out, then later closure of the fistula is feasible by invaginating the distal stumps of the intestine and returning them within the peritoneal cavity. This procedure, however, is not always satisfactory, and if it fails, the operation of complete exclusion is recommended.

Given a fistula, side-to-side anastomosis deep to the fistula is sometimes attempted as a step to aid in its closure. The performance of this procedure is hardly any easier than the performance of the complete exclusion operation, and is by no means as satisfactory, because the fecal stream is not completely diverted. If exclusion of any kind is to be recommended for fistula, it should be complete and not partial.

For acute intestinal obstruction. The exclusion operation is valuable for the treatment of acute obstruction of the small intestine, because it can effectively control the fistula which invariably follows exteriorization of nonviable intestine. Fistula from exteriorization is difficult to deal with, and is the reason stated by Cokkinis "responsible for the preference which many surgeons show for primary resection and anastomosis." Yet "exteriorization has a much lower primary mortality than the more radical method of immediate resection and anastomosis." The dis-



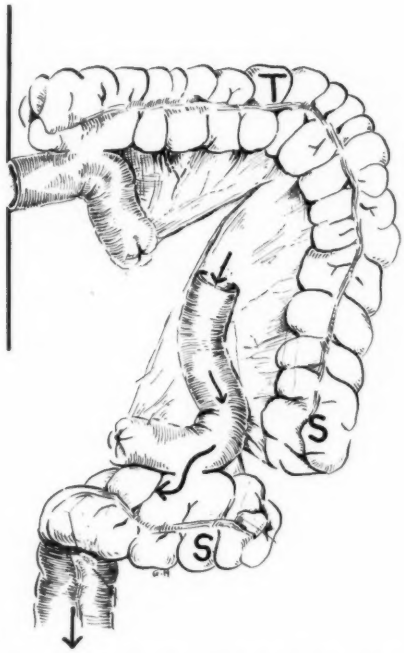


Fig. 5. The complete exclusion operation, Case 3. A, left, uncontrollable fistula following resection of the terminal ileum and right colon for regional enteritis. Marsupialization in the unjustified hope of closure by Mikulicz stages 3 and 4. B, operation concluded, fistula completely excluded by ileo-colostomy. Note that the sigmoid has been cut across and the ends inverted.

advantages of exteriorization are chiefly those incident to fistula, and diminish in proportion to the efficacy of the treatment of fistula.

Chemical balance. Restoring blood chemistry to normal before operating for fistula offers certain difficulties. Patients with fistula of the small intestine become debilitated due chiefly to the loss of the external secretions of the pancreas and liver. The proteins of the blood may drop; thus in patient 2 the total serum protein fell to 4.8 milligrams per cent and the patient developed nutritional edema just before the exclusion operation was performed. Immediately after the exclusion operation the proteins rose to 6.4 milligrams per cent and edema disappeared.

It is during the period when minor and often ineffective methods are being used in attempts to close a fistula that the blood chemistry is apt to become further altered despite supportive measures such as transfusion, etc. Often, indeed, it is not possible to bring the blood chemistry back to normal without closing the fistula. It seems preferable to perform the exclusion operation early and thus improve the blood chemistry by restoring intestinal continuity rather than delay in a vain hope that the chemistry can be restored before surgery is undertaken. Thus, looking back on the treatment of patients 1 and 2, it is felt that the exclusion operation should have been performed sooner, instead of waiting 22 days and 32 days as was done. By so delaying, patients 1 and 2 became almost hopeless operative risks.

INDICATIONS

The operation of complete exclusion can be used for fistula of the small intestine due to most causes. In this particular series, two of the fistulas were due to gangrene of the small intestine and followed the operation of exteriorization, and the other fistula resulted from terminal ileitis.

The principle of complete exclusion of the intestine is chiefly applicable to fistula of the small intestine, although it can be used for the large intestine. It cannot be used for fistula of the duodenum because exclusion of the duodenum

would result in the complete loss of the external secretions of the pancreas and liver, which is incompatible with life.

CONCLUSION

1. The operation of complete exclusion is recommended for the treatment of certain fistulas of the small intestine.

2. Its advantages are (a) it restores intestinal continuity as the first step, (b) it excludes the fistulous segment completely, (c) it is performed in a clean operative field, (d) the operation is surprisingly well tolerated even by debilitated patients.

3. The operation proved successful when other measures had failed in the treatment of three debilitated patients with fistula high in the ileum.

4. Two of these patients had been operated on for acute intestinal obstruction with gangrene of the small intestine. Exteriorization was used and the resulting fistula resisted closure by all measures short of complete exclusion.

5. The third patient had a fistula due to terminal ileitis.

6. The operation is not new but its application for fistula is unfamiliar.

7. If the operation is more widely used it may possibly cause a reduction in the mortality from acute intestinal obstruction due to gangrene of the small intestine, because it can effectively control the fistula which follows exteriorization.

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THE SURGICAL TREATMENT OF CHRONIC LYMPHEDEMA (ELEPHANTIASIS)

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OF the three circulating media, the lymphatic system has been the least thoroughly understood. The arterial circulation, with its visible pulsation, its early evidence of failure and its obvious importance to life, was the first to be studied. Its corollary, the venous system, on which the success of the arterial circulation depends, is anatomically and physiologically more clear. The lymphatic system, with a separate and complete circulation, resembles the venous system in that it eliminates tissue waste products, particularly the ones which the venous system does not remove. It connects with the veins at only two points: the important left and the less important right thoracic ducts, which enter the subclavian vein at its junction with the jugular vein. The lymphatic system is of prime surgical importance. Localization, absorption, and tissue response depend upon its adequate function. Surgical cure in malignancy requires the complete excision of the tumor and its primary extent to the neighboring lymphatics. The lymphatic system is not only important in diseases of other organs, but, in itself, it may be the site of disease processes. One such pathological syndrome, chronic lymphedema, or elephantiasis, has been a most difficult surgical problem.

TABLE I.—SURGICAL CLASSIFICATION OF LYMPHEDEMA

I. Amenable to surgical treatment
  1. Modified kondoleon procedure (as presented)
    a. Idiopathic
      1. Præcox
      2. Congenital or familial (Milroys)
    b. Acquired
      1. Trauma (accidental or surgical)
      2. Filiariasis bancrofti
      3. Occasionally the group secondary to venous pathology.
  2. Local surgical intervention
    a. Pressure—growth, etc.
    b. Traumatic or operative scars
    c. Most venous obstructions
    d. Local inflammation
    e. X-ray, radium and other burns
    f. Congenital lymph collections (Cystic hygroma, etc.)

II. Not Recommended for surgical treatment
  1. Mild idiopathic lymphedema
  2. Fungus infections
  3. Malignancies with invasion
  4. Allergic or systemic lymphedemas.

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Efforts to classify lymphedema on an etiological basis have not been too successful (Table I). To clarify the various groups, a surgical classification based on whether they might respond to surgical intervention has been prepared. The surgical intervention so considered is either local excision or the adaptation of a principle of resection of the superficial and deep lymphatic tissues, with application of the skin directly to the muscles—the so called Kondoleon principle.

The figures indicating incidence of various groups in the last 37 patients with lymphedema registered at the New York Post-Graduate Hospital are as follows:

Simplex or præcox form	10
Chronic phlebitis	10
Varicose vein pathology	6
Familial or Milroys type	2
Filaria	1
Infection	4
Epidermophytosis	1
Traumatic origin	3

In lymphedema, there is an occlusion of the lymphatic vessels, which may be of congenital origin, or may be due to pressure, inflammation, or thrombosis. As in other occlusions, fibrosis soon follows, with a permanent closure to drainage through these lymphatic vessels, thus establishing a vicious cycle. This process is accelerated by an increased protein content, which the work of Drinker and Fields and Homans demonstrated to be as high as 4 per cent, or one half that of the blood. The lymph accumulates in the tissue spaces of the involved area, with no method of escape. Elevation permits it to pass through the tissue spaces, to the contiguous normal area, where it is removed by unaffected vessels. Dependency causes repeated collections and with the increasing distention, the size of the affected limb increases. The leg becomes swollen, indurated, with pitting edema, and frequently secondary venous changes occur. The subcutaneous tissues become lymph spaces, ulceration may

occur, and a severe periodic febrile reaction is not uncommon.

The problem of surgical therapeutics in these cases has been one which has taxed the ingenuity of surgeons for over one hundred years. In mild cases, mere support is sufficient; the wearing of a rubber stocking, elevation for part of the day with a restricted activity, permits these patients to continue quite satisfactorily. Mecholyl by iontophoresis, suggested by Irving Wright, has relieved a very limited number in this group. In others, conservative measures are entirely inadequate and, with progression and periodic febrile reactions, many become economic liabilities.

The first operative effort, early in the Nineteenth Century (Les Francke) was with scarification, and Carnochans in 1851 used ligation of the iliac or femoral artery; both of these procedures resulted in many amputations. Dieffenbach and Mikulicz unsuccessfully excised subcutaneous tissues. Handley is credited with the development of the theory of draining obstructed areas through adjoining healthy tissue, using silk sutures as drains. Lang, Walther, Oppel, and Rosenaw all attempted modifications. Kondoleon, observing no lymphatic collections in the muscle, reasoned that the lymphatic blockage was entirely superficial and excised strips of intervening fascia with beneficial effects. Sistrunk, Kimura, Auchincloss, Knudson and Ghormley all added features to this original operative procedure. Homans contends that the beneficial effect of this type of operation is derived only through plastic excision of lymph collections, basing this thought on his failure to find muscle lymphatics and the presence of thrombosis of the iliac lymphatics (Table II).

We believe that much of the success of the operative removal of the superficial and deep fascia in these cases is due to the opening of a new avenue of lymph escape through the muscle lymphatics. Were this not true, the simple excision of superficial lymph tissue, such as was practiced by Mikulicz and Dieffenbach would have succeeded at times. We have performed biopsies at periods of from 6 to 18 months after this operation, which show a normal arrangement of tissue cells without replacement by lymphatic collections. If the results were due only to a plastic excision of lymph tissue, one would expect some degree of lymphatic accumulation to have recurred in the superficial tissues in this period of time. To augment drainage to contiguous tissues, we have prepared broad base pedicle skin grafts, thus permitting large skin areas to drain to neighboring healthy lymphatic tissue.

In the last 4 years we have performed the outlined operation on 12 patients and in a modified form 6 others have been so treated, and, despite the physiological and pathological processes on which relief is based, we can promise surgically an improvement in a high percentage of cases. Careful pre-operative and postoperative measurements in 6 extremities observed after the radical operation for from 1½ to 3½ years have shown a maintained reduction in the circumference of the leg from a minimum of 7 inches in 1 patient to a maximum of 21 inches in an advanced case, and our most recent patient had the circumference of his calf reduced from 55 inches to 25 inches.

TABLE II.—OPERATIVE RESULTS IN CHRONIC LYMPHEDEMA FROM THE LITERATURE (KONDOLEON PRINCIPLE)

Surgeon	Number cases	Results good	Results fair	Not improved
Kondoleon	6	Not too satisfactory		
Burke	16	6	2	4
Sistrunk	40	30		10
Kimura	9	9		
De Gaetana*				
Torgenson	5	5 (6 months)		
Del Toro & Pons	18	6	6	4†
Kuntzen	16	8	4	3
Ghormley-Overton	64 (55 followed)			12.5
	87.5% (56)			(8)

*Good results with Sistrunk's method.
†Not followed.

TECHNIQUE

1. Pre-operative preparation. A minimum of 2 weeks' hospitalization is required, during which time the leg is elevated and diuretics, usually in the form of the mercurials, are administered. The fungus infection, which as a rule accompanies this process, is controlled. Sulfanilamide is prescribed prophylactically for several days prior to operation. This drug has been used empirically. Drinker and Fields showed in their work on experimental elephantiasis in dogs, that each time the febrile reaction occurs, streptococci could be cultured from the lymph, and it is in an effort to eliminate these organisms that the sulfanilamide is used. Careful measurements of the circumference of both limbs are recorded. For 2 days prior to operation a careful skin preparation, consisting of green soap and alcohol cleansing and the use of sterile drapes, is carried out.

2. Operation. Under prolonged spinal anesthesia (pontocaine) an elliptical incision is made in the lateral aspect of the thigh from the iliac crest to the femoral condyle. Below the knee this elliptical incision is continued posteriorly in the calf to its lower margin, when it again runs laterally to the external malleolus. This type of

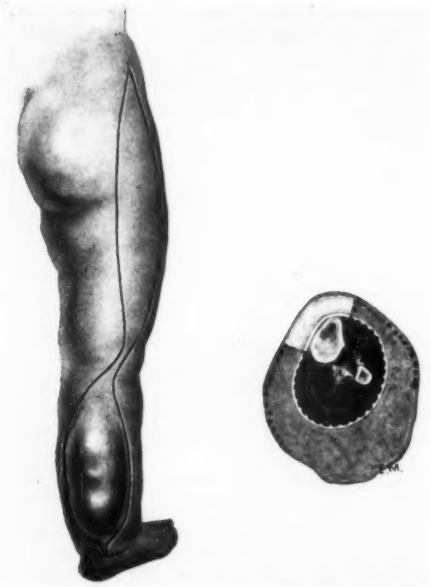

Fig. 1. Outline of incision. The skin is undermined for 75 to 100 per cent of the leg's circumference. The superficial and deep fascia with the outlined skin is removed *en masse* from 75 to 100 per cent of the leg. Cross section: shaded area outlined by dots shows section of skin, superficial and deep fascia to be removed.

incision exposes the area of greatest lymph collection (Fig. 1). In selected instances the incision is modified to run entirely laterally (Fig. 2).

Fig. 2. Alternate incision showing outline before and after operation. Cross sections illustrate area to be excised and re-application of skin directly to the denuded muscles.

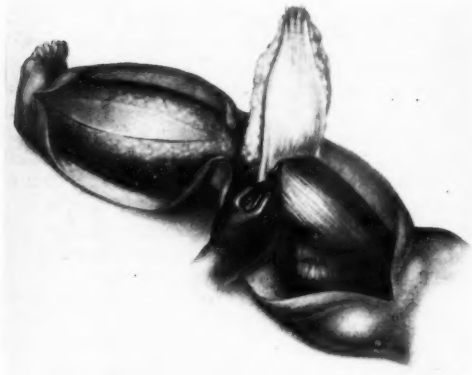

Fig. 3. Outlined skin, superficial and deep fascia being removed *en masse* from two-thirds to the total area of the leg.

A sufficient ellipse is incised to allow the residual skin, when approximated, to equal the circumference of the normal limb. The skin alone then is undermined until three-fourths of the circumference of the leg has been exposed; this is done without transverse incisions, which would produce further scars. The incision is then carried through the superficial tissue and the deep fascia throughout three-fourths of the circumference of the leg and a block of tissue, which includes the ellipse of skin and the three-fourths circumference of the superficial and deep fascia, is excised *en masse*. Bleeding is controlled, the skin is then united with interrupted alloy steel wire, and directly approximated to the denuded muscle. The insert in Figure 1 and Figure 2

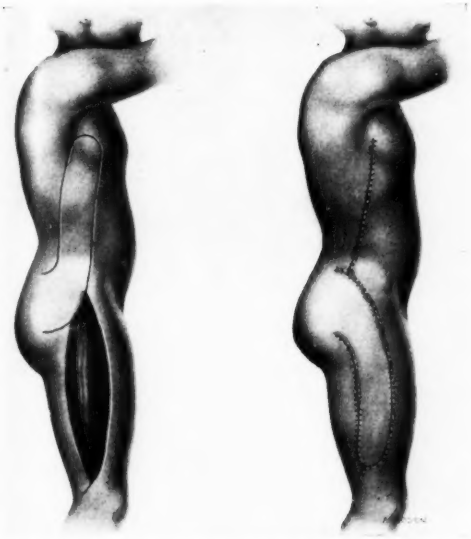

Fig. 4. The broad base pedicle skin graft is used to replace excised diseased skin. Skin lymphatics may thus drain through the broad base to contiguous healthy tissue.

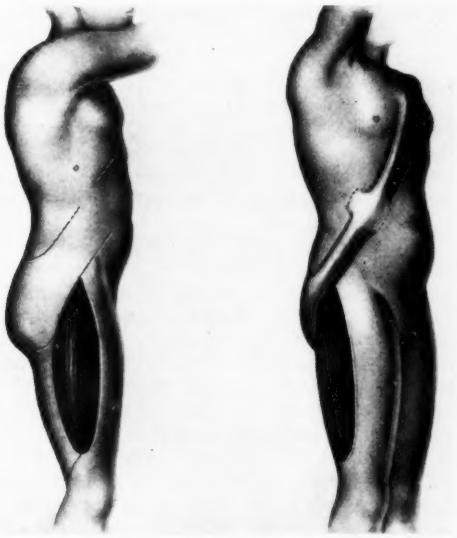

Fig. 5. Broad based pedicle tube graft being prepared, with the base in the buttocks above the area of skin lymphatic blockage.

illustrates in cross section by the dotted lines the tissue excised and remaining after the plastic closure. In our latest cases we have removed 100 per cent of the fascia—thus entirely encircling the limb.

In instances in which the skin had become devitalized by constant overstretching, it was necessary partially or completely to remove it. The split and full thickness skin grafts, which were

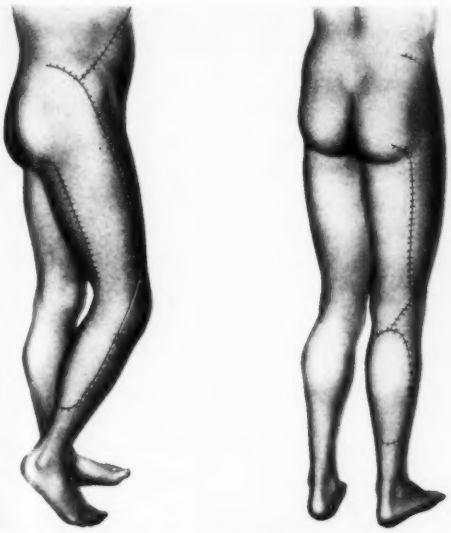

Fig. 6. First figure shows the graft in place, and second figure after plastic operation to complete leg extension.

Fig. 7, left. Pre-operative photograph of a male, aged 21 years, with congenital lymphedema. Leg circumference before elevation, 35 inches.

Fig. 8. Same patient 3 months after operation. Follow-up of 3 years shows reduction in leg circumference maintained despite active daily work.

first used, were replaced by the more satisfactory broad based pedicle tube grafts. It was found then that in addition to skin replacement, the pedicled graft would drain the skin lymphatics and thus have a new method of aiding skin lymphatic drainage. Inasmuch as the tubes are made 5 inches in width, the drainage factor becomes an important one. This skin graft, as shown in Figures 4 and 5, is an important addition to the operative treatment.

3. Postoperative care. The limb is maintained in an elevated position for approximately 3 weeks, after which time the patient is gradually permitted to lower the leg and bear weight, always with support. When necessary, the secondary plastic operation after the graft is performed. After-care consists of support for 6 months, when the bandages may be removed gradually, dependent upon swelling. It is well to emphasize the fact that this is a chronic circulatory disease and that subsequent support at times may be found necessary.

POINTS TO EMPHASIZE

We would emphasize the careful selection of the patient, the pre-operative preparation, spinal anesthesia as the anesthetic of choice, the measuring of the circumference of the leg, the radical undermining of at least three-fourths of the circumference of the leg, care to prevent constriction at the joint, and the use of steel wire to reduce reaction. Our more recent work with the broad base pedicle skin graft to replace the widely excised diseased skin seems even more satisfactory. Blood transfusion has reduced the incidence of operative shock. By being sufficiently radical a second stage operation on the opposite side of the leg has been eliminated. In only one instance has there been a slough and that was over the dorsum of the foot, where the desire for a better cosmetic result caused too great undermining. This had a recurrent lymphedema, and the previous scars were a factor. The deep fascia had regrown since a previous, much less radical, operation at another institution 5 years before.

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THE DECREASING MORTALITY OF APPENDICITIS

SO much has been written and said about the increasing mortality of appendicitis that such statements have been accepted widely. But if the latest figures available are examined closely, some doubt arises about the validity of this conclusion. According to the figures compiled by the United States Bureau of the Census, the death rate from appendicitis has decreased progressively and significantly from 1930 to 1937, —the last year for which figures are available. The reported mortality rate of appendicitis per 100,000 population in the United States was 15.3 in 1930; 15.2 in 1931; 14.2 in 1932; 14.1 in 1933; 14.3 in 1934; 12.7 in 1936; and 11.9 in 1937, or a reduction of 28.7 percent in seven years! According to the statistical bulletin of the Metropolitan Life Insurance Company, this trend continues.

Moreover, if the figures prior to 1930 are analyzed critically, there is considerable evidence to show that the incidence and the mortality rate from acute appendicitis have remained stationary or at least have not been increasing for an even longer period of time.

Perhaps one of the most careful and most widely quoted compilations of the death rate of acute appendicitis is that of Hoffman, which appeared in the *Spectator* in 1933. He concluded that in the *sixty largest cities of the United States* the appendiceal death rate has been increasing. For the country as a whole, however, in 1933, Hoffman says, "For all practical purposes the death rate has reached a stationary condition with a slight tendency downward." The death rate in the sixty largest cities had increased but this is not, however, in our opinion, a true index for the country as a whole. It does not take into consideration the enormous increase in hospital facilities and the even greater increase in the number of patients hospitalized, in the last fifty years. According to figures compiled by the American Medical Association there were fifty thousand hospital beds in the United States in 1872. In 1909 there were 421,000; in 1918, 612,000; in 1928, 892,000; and in 1937, 1,124,000—or a twenty-fold increase in 55 years. Hospitals are located in the larger cities, but the patients who occupy hospital beds may come from the city itself or the surrounding countryside, and the number of deaths reported from hospitals may represent a much larger area of population than the cities reporting. Just because more people die from appendicitis in the hospitals of the sixty largest cities of the United States (which is correct), may not, of necessity, indicate that the incidence and mortality of appendicitis are increasing in the United States as a whole. It may mean only that more people go to the hospital each year. In-

deed, the ratio of the total number of patients admitted with appendicitis to the total number of hospital admissions has decreased.

Prior to 1930, the *reported* mortality rate from acute appendicitis increased from 9.7 per 100,000 population in 1900, to 15.3 per 100,000 in 1930. These figures might reflect any one or a combination of more than one of three separate and distinct trends, i.e., more accurate diagnosis, increased fatality rate, or increased incidence of appendicitis. From the evidence at hand, it would seem reasonable to assume that more accurate diagnosis has played a major rôle in almost doubling the reported death rate of appendicitis, from 1900 to 1930. Not only has medical diagnosis become more accurate during these years, but the average patient has had more adequate medical attention coincident with the shift in population from rural to urban areas. Diagnosis has been further facilitated by this great increase in the number of patients hospitalized during this period, with the increased opportunity for consultation, laboratory procedures, and particularly postmortem examination which hospitals offer.

Then, too, education of the medical profession to recognize appendicitis, except in the large medical centers, was slow, so that deaths from this disease were either erroneously classified or included in the group, "Death from unknown or ill-defined causes." Even today in certain isolated sections of the country, "inflammation of the bowels" is a more popular diagnosis than "acute appendicitis." In any event, while the reported death rate from appendicitis increased only 5.6 per 100,000 population from 1900 to 1930, the reported death rate from unknown and ill defined causes decreased from 73.8 per 100,000 population in 1900 to 21 per 100,000 in 1930. In other words, from 1900 to 1930, 52.8 deaths per 100,000 population or almost ten times the increase in the number of deaths attributed to appendicitis were removed from the category of "Unknown and ill-defined causes" and correctly classified. As those "unknowns" were reclassified the number of deaths assigned to every other cause was increased, and it seems reasonable to assume that the relatively new and unfamiliar disease "appendicitis" was a major recipient.

In any event, the mortality rate from appendicitis in the United States as a whole has not increased but has decreased significantly in the past 10 years. And although we do not believe the present record to be an ideal one, we are encouraged to note this significant reduction in the ravages of "intraperitoneal enemy number one," and we feel confident that this trend will continue due to the continued campaign for education of the lay public and the continued campaign for improvement in the standards of surgical and hospital care. WOOLFOLK BARROW.

LOCAL TREATMENT OF THE BURNED AREA

"It is a balsam," answered Don Quixote, "the receipt of which I have in my memory, with which one need have no fear of death, or dread dying of any wound." ... "If that be so," said Sancho Panza, "I renounce henceforth the government of the promised island, and desire nothing more in payment of my many and faithful services than that your worship give me the receipt of this supreme liquor."

DESPITE a great amount of careful experimental study and clinical observation, the problem of the nature of burn toxemia is still unsettled. There is no general agreement as to whether there is a burn toxin and if there is, as to its nature, and still less agreement as to the source of the toxin if we concede for sake of argument that such a product is present. Efforts directed toward the local treatment of a burn based upon the assumption that the source of

the burn toxemia is the burned tissues met with such an improvement in results that the conclusion seemed almost inescapable that the premise must be correct. Davidson's tannic acid therapy for burns has become universally adopted. When carried out as advocated and as has been repeatedly stressed by such men as Penberthy and McClure who had close contact with Davidson, the treatment yields most excellent results.

However, observations of many cases treated with tannic acid without the careful preliminary cleansing stressed by the originator of the method have shown that disastrous results may follow. It has become obvious that simply to coagulate the dead protein of the burned surface is not enough but that some other factors are important. Various antiseptics or rapidly tanning agents have been added to, used in conjunction with, or substituted for, tannic acid, but none has been more successful than tannic acid.

It is instructive to disregard for the moment those factors in burns about which our knowledge is incomplete and to look upon a burn simply as a large open wound in which the tissues are badly damaged and seriously handicapped both in reparative powers and in resistance to bacterial invasion. Associated with such a wound we would also anticipate shock, a phenomenon as perplexing as that of burn toxemia but for which we have certain fairly satisfactory methods of treatment. I mention the question of shock only to complete the analogy between burns and other open wounds.

Let us follow such an injury from the time of its inception to that of its definitive care, forget that we are dealing with a burn, and simply think of the injury as a large open wound which is receiving the care so often accorded a large burn. When this injury occurs, it is usually under circumstances of great flurry and excitement. The patient, fully clothed, often with the wounded area and covering clothes soiled, sustains a painful injury into which dirty clothing and contaminants from the skin are immediately deposited. Someone, in order to stop the action of the traumatizing agent, may roll the victim in a rug or some other contaminated material. Unless the wound is too serious, a well meaning friend or neighbor or parent smears the surface with butter or soda or lard or one of the various proprietary ointments recommended in advertisements for first aid treatment for burns. The patient is then brought to the hospital in an ambulance, often wrapped in another blanket and is deposited in the emergency room. From the time of the injury to the arrival in the emergency room, the wound has been taken care of by one or more individuals none of whom is masked and all of whom have directly or indirectly contaminated the raw area with unsterile hands, expired droplets, ointments, and dressings. In the emergency room, the wound is uncovered and examined by several persons. If there is no apparent shock or if the shock is not too marked, a hypodermic of morphine is administered and treatment of the wound is started. Masks and caps and sterile gloves are usually lacking. The clothes are cut from the patient, and the wound is exposed and again examined. Adherent dressings and clothing are picked off, and the raw area is then covered with another ointment or preparation is made for tanning it. If it is to be tanned, the patient is placed on a sterile sheet, a light cradle is placed over him, and someone delegated to spray the area with tannic acid solution every 20 to 30 minutes until "done." This process may require 12 to 24 hours during which time the open wound is exposed to the air, partially protected from contaminants by the coverings of the light cradle and by a crust

which rapidly becomes impervious but is still subject to cracking with consequent exposure of the surface. If cracks appear in the crust even after 24 to 48 hours, the spray is again used on them and the area is again tanned. Where ointments have been used, dressings are applied over them, and these are removed daily or every few days to allow the re-application of more of the magic salve.

If we look upon this injury as an open wound forgetting that it is also a burn, we are not surprised to learn that a very high percentage of victims develop serious infection, that the wounded areas take weeks and months to heal, and that mortality rates tend to be very high. Nor are we surprised if secondary contamination occurs during the frequent dressings which usually mark the course of an extensive burn.

In this theoretic imaginary wound one factor which has been insufficiently considered is that of the contamination of the large raw surface. The aim has been to cover it with *something* as rapidly as possible, ignoring the fact that the surface is already liberally contaminated with dirt and bacteria, and is susceptible to further contamination with bacteria from the nose and throat of everyone who examines it. To treat such a wound without first thoroughly cleansing it violates not only the principles of good surgery and the tenets laid down by Davidson but also speaks for a faith in tannic acid or some well advertised ointment exceeded only by that evidenced by Don Quixote in the balsam of Fierabras.

Let us disregard for the moment any conception whatsoever concerning burn toxins and simply conceive of a burn as a large open wound. Our ideas concerning its management at once change, and our initial efforts in dealing with it are directed toward cleansing the surface of as many contaminants as possible, of removing as much débris as can be removed, and of covering the area as quickly as possible with a sterile protective dressing. The burn may be cleansed as any other open wound with soap and water and liberal flushings with normal salt solution. While this is being done, every possible precaution is taken to prevent bacteria from nose and mouth and other objects from gaining entrance to the wound. Caps and masks should be worn by every one who takes part in the cleansing or who comes into the room during the process. As strict an aseptic technique should be followed as in the operating room. Hands should be scrubbed and covered with sterile rubber gloves; instruments and dressings should be sterile, and an attempt made to complete the cleansing and dressings at the earliest possible moment. As for the coverings for the wound, there are only two prerequisites; first, that they be nonirritant and, second, that they adequately protect the surface and prevent fluid loss from it. A large pressure dressing similar to that applied over skin grafts seems to be advantageous in that it helps to immobilize the part and minimizes the loss of fluids into the tissues about the burn. If the burns affect the extremities, splints should be used to provide rest for the injured part while for burns of the trunk we would rely mainly upon nature's efforts to splint it. The shock that accompanies such a wound and the protein and electrolyte imbalance that may occur may be controlled by the usual measures of warmth and sedation, and the administration of fluids in the form of blood or plasma transfusions, saline and glucose.

If this conception of a burn as a wound is correct, it should not matter much just what the covering agent is. If we can get the raw surface quickly covered with a tannic crust and not expose the wound for too long a time while doing so and keep the crust from cracking or constricting or traumatizing the skin at

its borders, we will have a satisfactory dressing. If there is available some other type of dressing which is more rapidly applied and does not have the disadvantages of a brittle crust, there should not only be no reason for not using it but certainly definite advantages in doing so. Equally admissible should be the conclusion that the burned area is a raw surface susceptible to contamination for as long a time as it remains open. Dressings subsequent to the one applied following the initial care should, therefore, be reduced to a minimum in number and should be carried out with strict aseptic technique. The use of unsterile salves and irritant chemicals would find no more application in the burn than in a compound fracture.[1]

[1] In the children's wards at Cook County Hospital in Chicago, the mortality rate from burns has been reduced from 10 per cent to 3.9 per cent by a method of treatment such as that which is outlined here: Careful soap and water cleansing, and a pressure dressing over vaseline gauze (personal communication, Dr. Harvey S. Allen).

It has seemed to me that the emphasis in the care of burns were better placed on their character as open wounds than on some agent which is to be applied to the surface. Davidson's great contribution to surgery, namely the demonstration that a burn may be cleansed and closed the same as any other open wound, has been transformed into a plea for tannic acid. If it appears that closure may be more effectively accomplished, after careful soap and water cleansing, with simple sterile vaseline strips and large amounts of dry gauze snugly bandaged over the burn, it does not detract a whit from the monumental contribution made by Davidson. It is the principles that count in surgery; and if they can be shown to apply to burns as they do to the treatment of any other open wound, a tremendous service has been rendered.

MICHAEL L. MASON.

TEXTS AND DOCUMENTS

ARNO B. LUCKHARDT, M.D., Chicago, Illinois

EVEN the medical man who is a staunch adherent of Methodism is probably unfamiliar with the fact that the Rev. John Wesley wrote a book on medicine. According to Arnold Lunn[1], one of his biographers, John Wesley "distrusted doctors, and was never happier than when prescribing for his friends. . . ." "I thought," he says,[2] "of a kind of a desperate experiment. I will prepare and give them physic myself." The book published first in 1747 is entitled: *Primitive Physic or An Easy and Natural Method of Curing Most Diseases*, by the Rev. John Wesley, A.M., Late Fellow of Lincoln College, Oxford. His suggestion that "*The Primitive Physic* should be in every family" was with his other literary output for his followers tantamount to a command to buy. Best seller Wesley made a lot of money from his literary output which money was given away.

The command to buy his books probably accounts for the numerous editions of his *Primitive Physic*. The twenty-eighth edition of this book, a small duodecimo volume of 108 pages was published at London in 1815 and "sold by Blanchard, 14 City Road; and at the Methodist Preaching Houses in town or country."

The original preface to the work of 1747 is repeated with a postscript dated 1755 and two subsequent introductory remarks with respect to additions and corrections dated 1760 and 1780, respectively. It is from this twenty-eighth edition that excerpts are taken as items of interest in this curious book designed as guide to families experiencing sickness or diseased conditions. This volume on domestic medicine was treated analytically by George Dock.[3] This is decidedly not my intention. Having been serious for the most part, in this series, I thought it time to introduce something that would amuse the modern physician and by direct quotation cause him possibly several chuckles. The body of work is arranged in encyclopedic (alphabetical) form beginning with "*Abortion*," "*Ague*," "St. *Anthony's* Fire" and ending with "Emetic Tartar *Vomit*," "Water Drinking," but the last subtitle lists out of alphabetical sequence, "Electrifying, and Fasting Spittle."

The last sentence is a "plug" for he advises "all, in or near London, to buy their medicines at the Apothocaries Hall. There they are sure to have them good."

Quoting general health rules from Dr. George Cheyne he gives receipts for various ailments some of which, to inspire confidence of the reader in their effectiveness, he marks with an asterisk. The ensuing quotations from this book are reprinted for their curious and perhaps mirth producing quality:

"Malt liquors (except clear, small beer, or small ale, of due age) are extremely hurtful to tender persons."

"But I still advise in complicated cases, or where life is in immediate danger, let every one apply to a Physician that fears God. From one who does not, be his fame ever so great, I should expect a curse rather than a blessing."

"For an Ague Apply to the stomach, a large Onion, slit."

"To cure Baldness. Rub the part, morning and evening, with onions, till it be red; and rub it afterwards with honey. Or, wash it with a decoction of boxwood; Tried. Or electrify it daily."

"A Cancer in the Breast. Take Horse Spurs (warts that grow on the inside of the horse's forelegs) and dry them by the fire, till they beat to powder. Sift and infuse two drachms in two quarts of ale; Drink half a pint every six hours, new milk warm. It has cured many. Tried. Or, apply goose dung and celandine, beat well together and spread on a fine rag. It will both cleanse and heal the sore."

"Children. No child should touch spirituous or fermented liquor, nor animal food, before two years old."

"For Chin Cough or Hooping Cough rub the back lying down with old Rum. It seldom fails."

[1] John Wesley. By Arnold Lunn. The Dial Press, New York 1929, Longmans Green & Co., Toronto.
[2] Loc. cit. p. 190.
[3] The Primitive Physic of Rev. John Wesley. By George Dock, M.D., J. Am. M. Ass., 1915, 64: 629-638.

"For Consumption. Turn a pint of skimmed milk with a half a pint of small beer. Boil in this whey about twenty Ivy leaves, and two or three sprigs of hyssop. Drink half over night, the rest in the morning. Do this, if needful, for two months daily. This has cured in a desperate case. Tried."
"For dull sight drop in two or three drops of juice of rotten apples often."
"For 'iliac passion' meaning 'a violent kind of cholic in which the excrements are supposed to be thrown up by the mouth in vomiting' [fecal vomiting in acute intestinal obstruction or appendicitis?]:—
"Hold a live Puppy constantly on the belly (Dr. Sydenham)."
"For Sore and Running Legs Poultice them with rotten Apples. Tried. But take also a purge or two every week."
"Quinsy may be treated by applying a large White Bread Toast, half an inch thick dipt in brandy, to the crown of the head, till it dries."
"For stitch in the Side apply Treacle spread on a hot Toast. Tried."
"Use no violent diuretics for 'Stone.' Mead is a proper drink."
"To Stop Vomiting Apply a large Onion slit across the grain to the pit of the stomach. Tried."

Dr. Wesley's book ends with the marvelous efficacy of "fasting Spittle" when outwardly or inwardly applied. When outwardly applied it has relieved or cured "blindness, corns, fresh cuts, deafness, scorbutic tetters, sore legs and warts." Given inwardly it relieves or cures "asthmas, cancers, falling sickness, Gout, gravel, palsy, scurvy, stone and swelled Liver."

Enough has been cited to indicate the curious character of the Rev. Wesley's therapeutics; more will occur to the contemplative reader in connection with Wesley's reference to the use of ale, rum and mead.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

WHEN in a volume there converge thorough scholarship, seasoned experience, and a gift for clear prose, the happy result is a textbook such as *Diseases of the Nervous System*.[1] That labyrinth which constitutes clinical neurology is here illumined in such a manner that a beginner in addition to assimilating the material might even find it palatable.

The opening chapters give an adequate review of the anatomicophysiological considerations necessary for the understanding of neurologic function and dysfunction; then the various disease entities are described in a systematic and pithy fashion. This edition includes discussions of recent developments in neurology such as the psychological manifestations of organic disease, electro-encephalography, and the rôle of vitamin deficiency in nervous disorder. Other topics of timely interest deal with the neurotropic viruses and the chemistry of muscle and humoral factors in the transmission of nerve impulses at the myoneural junction.

This work is undoubtedly one of the best textbooks of neurology extant. Its usefulness is not exhausted with the beginner; graduate student, teacher, and practitioner will all find it a clear and succinct guide to their experiences in clinical neurology. HARRY A. PASKIND

[1]DISEASES OF THE NERVOUS SYSTEM. By W. Russell Brain, M.A., D.M. (Oxon.), F.R.C.P. (London). 2d ed. London: Oxford University Press, 1940.

IN a previous publication in textbook form, Dr. Hugo Roesler[1] has set forth the theory and practice of radiology of the cardiovascular system, giving a number of short case reports as examples. The present atlas of 125 pages, of 10 by 13 inch size, and 166 illustrations presents a comparative study of the roentgen and the postmortem findings. Stress is laid upon the changes in form and structure of the heart, the great vessels, and the lesser circulation as revealed by the x-ray studies. The case reports include many types of disease but particularly the most common cardiovascular affections. The presentation correlates the roentgenological method with electrocardiography, ophthalmoscopy, and the clinical and laboratory studies. Particularly helpful are the large size cuts, many of them clarified by line drawings and photographs of whole specimens and of sections. The workmanship of the book merits high praise. It is really a pleasure to study a book whose illustrations are, in the first place, of such high excellence and, in the second place, so beautifully reproduced in the text. This is a very satisfactory publication. JAMES T. CASE

[1]ATLAS OF CARDIOROENTGENOLOGY. By Hugo Roesler, M.D., F.A.C.P. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1940.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

FOREIGN BODIES LEFT IN THE ABDOMEN; THE SURGICAL PROBLEMS; THE LEGAL PROBLEMS. By Harry Sturgeon Crossen, M.D., and David Frederic Crossen, LL.B. St. Louis: The C. V. Mosby Co., 1940.

LIPIDOSES: DISEASES OF THE CELLULAR LIPID METABOLISM. By Siegfried J. Thannhauser, M.D., Ph.D. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D. (Hon.), F.A.C.P., Hon. F.R.C.P. (Can.). Reprinted from Oxford Loose-Leaf Medicine. London, New York, Toronto: Oxford University Press, 1940.

THE ENDOCRINE FUNCTION OF IODINE. By William Thomas Salter. Cambridge, Mass.: Harvard University Press, 1940.

DIAGNOSIS AND TREATMENT OF MENSTRUAL DISORDERS AND STERILITY. By Charles Mazer, M.D., F.A.C.S., and S. Leon Israel, M.D., F.A.C.S. New York and London: Paul B. Hoeber, Inc., 1940.

A FAMILY DOCTOR'S NOTEBOOK. By I. J. Wolf, M.D. New York: Fortuny's, 1940.

TREATMENT IN GENERAL PRACTICE; SURGERY (Continued). Articles republished from the *British Medical Journal*. Vol. 4. London: H. K. Lewis & Co. Ltd., 1940.

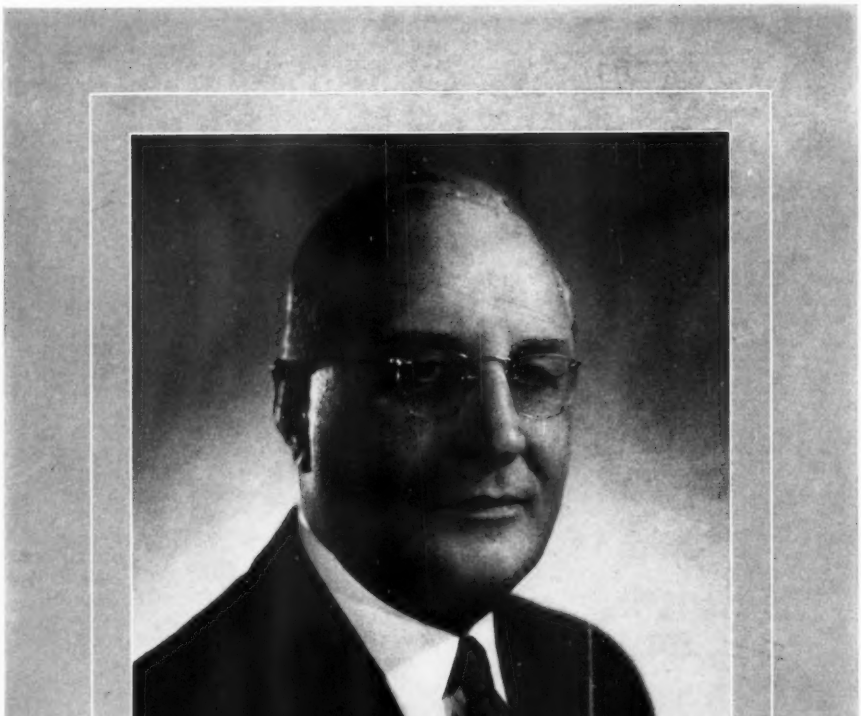
THE MERCK MANUAL OF THERAPEUTICS AND MATERIA MEDICA. 7th ed. Rahway, N. J.: Merck & Co., Inc., 1940.

IN SEARCH OF COMPLICATIONS. An autobiography by Eugene de Savitsch, M.D. Foreword by Arthur Krock. New York: Simon & Schuster, 1940.

A SURGEON EXPLAINS TO THE LAYMAN. By M. Benmosché, M.D. New York: Simon & Schuster, 1940.

DIAGNOSIS AND TREATMENT OF ARTHRITIS AND ALLIED DISORDERS. By H. M. Margolis, M.D., M.S., F.A.C.P. New York and London: Paul B. Hoeber, Inc., 1941.

CLINICAL PELLAGRA. By Seale Harris, M.D. Assisted by Seale Harris, Jr., M.D. Foreword by E. V. McCollum, Ph.D., Sc.D., LL.D. St. Louis: The C. V. Mosby Co., 1941.



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ASEPTIC RESECTIONS IN THE GASTRO-INTESTINAL TRACT

With Special Reference to Resection of the Stomach and Colon

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SATISFACTORY methods of establishing intestinal continuity after resection by the closed or aseptic method have been available for over 30 years. It is only within the last decade, however, that the closed method of anastomosis has acquired converts in any numbers. The Parker-Kerr (1908) basting stitch excited the interest of a number of American surgeons in the closed methods of intestinal anastomosis, and the growing concern displayed by surgeons in the past decade in aseptic anastomoses may in a sense be said to be cumulative. The development of special clamps to facilitate performance of the anastomosis by Rankin and Stone have accelerated considerably wider acceptance of the closed method.

Yet, within the past year, two well-known American teachers of surgery fathered a textbook on operative technique and failed to describe the closed method of anastomosis. This occurrence, I believe, mirrors fairly accurately the attitude of a large body of surgeons toward the closed anastomosis. A few surgeons, while insisting that the closed anastomosis be employed in establishing intestinal continuity after resection in the colon, feel no necessity for employing the same method in establishing intestinal continuity in the small bowel. A larger number cling to the open anastomosis just as they embrace all the worthwhile traditions of the past. A number of those, however, who are in a position to influence the opinions of others are inclined, I fear, to look upon the closed anastomosis as an unnecessary refinement or perhaps even as the figment or fetish of surgical dilettantes. Those familiar with the advantages and niceties of the closed anastomosis recognize that the method meets fully the requirements of clean, exacting surgical technique, embodying sound principles of architectural reconstruction. Those who scoff at the closed or aseptic anastomosis need our compassion more than they deserve our censure, for they are probably unaware that they, like the open anastomosis, are sliding backward, perhaps imperceptibly, yet definitely.

My apostasy from the open method of anastomosis is relatively recent, though for more than 2 years I have made only closed anastomoses in the gastro-intestinal tract. I confess freely that my enthusiasm for the closed anas-

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tomosis may partake of the zealous fervor of a proselyte for his new sect. Yet, an enlarged experience has not diminished this ardor, but, on the contrary, has strengthened the conviction that satisfactory continuity after segmental resections can be established in the gastro-intestinal canal with less risk to the patient by the closed than by the open method of anastomosis.

THE TECHNIQUE OF CLOSED ANASTOMOSIS

Somewhat more than a year ago I described a method of closed anastomosis adaptable to any segment of the alimentary canal. It was proposed, in particular, to describe a technique for establishing gastrojejunal continuity by the closed method following gastric resection. Satisfactory anastomoses employing the method have been made between the esophagus and jejunum, stomach and jejunum, as well as between segments of small intestine and colon. The method is adaptable to end-to-end, end-to-side, or side-to-side anastomoses. The instrumentarium and technique are simple though the latter is, of necessity, somewhat more precise and exacting than that of the open anastomosis. The time consumed in making the anastomosis, particularly the gastrojejunal anastomosis, is somewhat longer than that of the open operation in which running sutures are employed largely—a consideration declared by some surgeons to be of great importance, but a matter which, as far as my experience goes, is of no consequence to the patient, whose interest in the operation is to be regarded as paramount.

The technique of anastomosis is essentially the same, no matter what tubular segments are to be approximated. Briefly told, two rows of interrupted sutures are placed posteriorly, the most posterior row being placed first and the interrupted plain quilt mattress suture of Halsted being used. The suture nearest the clamp, both behind and anteriorly, is of the Cushing variety. Finally, a row of Halsted mattress sutures is placed anteriorly, completing the anastomosis.

The advantage of the instrument described by the writer patterned after the Martzloff intestinal clamp is that it provides the superiority and adaptability of two clamps for the posterior row, permitting rotation of the clamps as becomes necessary in accomplishing the approximation. A ferrule is applied to the distal end of each blade (Fig. 9) as the instrument is closed to insure and maintain satisfactory coaptation of the thin jaws of the clamps. On completion of the two posterior rows of sutures the two clamps are then rotated in an axis of 180 degrees and are apposed securely by a double ferrule at the end and by a tightening device over the handles, preparatory to placement of the anterior rows of sutures. One has, therefore, at his disposal two clamps held separately for the posterior suture and two clamps held rigidly as one instrument for the easier anterior suture.

Latterly, a running suture of fine chromic catgut (No. 000) has been employed posteriorly as well as anteriorly in the row next to the clamps. After withdrawal of the clamps, the anterior and posterior catgut sutures are tied to each other at both ends of the anastomosis. As before, a row of Halsted mattress sutures of fine silk (Deknatel D test strength, 2.5 pounds) is employed in the first posterior and the last anterior row. The finding of an occasional silk stitch dangling from the gastrojejunal anastomosis a few months after the operation by the gastroscopist persuaded me to make this trial. However, at the same time the running suture approximation near the clamp reduces the time necessary for performing the anastomosis materially. This method of procedure has been eminently satisfactory and will prove probably more practical than anastomosis by interrupted sutures alone. I have had no occasion to doubt that a satisfactory mucosal approximation could be achieved by this method of anastomosis. An experimental study to appraise the mode of mucosal healing after gastrojejunal anastomosis with reference to the time factor in both open and closed anastomosis would appear to be worth while.

In side-to-side anastomoses, the portion of the viscus engaged above the clamp is not cut off with the cautery until the posterior sutures have been placed. The surgical diathermy is employed only on the stomach, 2 to 3 seconds (stop watch) of a moderately strong coagulating current sufficing to insure satisfactory

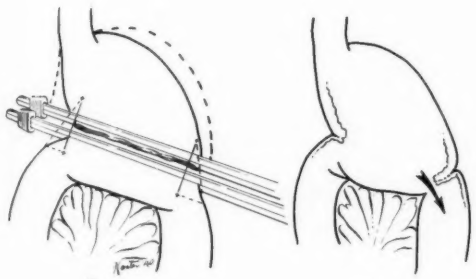


Fig. 1. My conception of the usual cause of obstruction at the efferent outlet after gastrojejunal anastomosis (antiperistaltic) in the Hofmeister plan of gastric resection. a, The surgeon should be careful to place his sutures in the jejunal wall at the *X* mark. If he takes more of the readily available jejunum than he should (as shown in the triangulated area), of necessity considerably more tissue will be inverted than the surgeon intended, with ensuant narrowing of the efferent outlet. In the Hofmeister plan of procedure (antiperistaltic), on the afferent side, narrowing of the inlet does not accompany this oversuturing because inverted gastric wall is approximated to the triangulated jejunal wall without compromise of the stoma. b, The effect on the efferent side is obvious. In addition to the consideration just described, it is important to place the sutures near the clamp. It is my plan to place the first posterior row less than 1 centimeter from the clamp. If this plan is adhered to rigidly, no more tissue will be inverted by the closed method than in the open anastomosis.

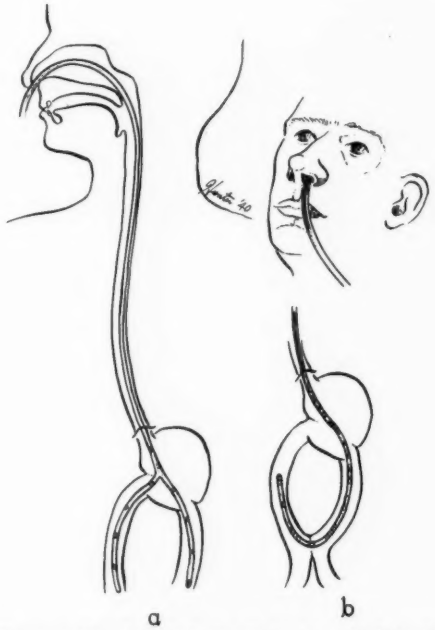


Fig. 2. a, Use of the forked catheter to avoid distention of the afferent loop after gastrojejunal anastomosis. The 2 forks are tied together at the tip and the tube may be passed through the nostril without difficulty into the stomach. When operating for gastro jejunal ulcer, I attach an extra segment of catheter to the proximal fork and place it proximal to the oblique end-to-end jejunal anastomosis necessitated by detachment of the gastrojejunostomy. b, Use of a straight catheter for the same purpose when entero-anastomosis is made. Avoidance of distention of the proximal jejunal loop is probably an important item in gastric resection.

hemostasis. A metric rule is employed invariably to determine the exact lengths of the segments engaged in the clamps for the anastomosis to obtain absolute parity in length. The gastrojejunal anastomoses have been 6 centimeters and lateral anastomoses in the small or large intestine have been between 4 and 5 centimeters in length. A preliminary crush of the wall, prior to placement of the thin, narrow-bladed aseptic anastomosis clamp is employed only in the stomach, where great vascularity demands painstaking hemostasis. The large gastric crusher employed initially has been replaced by the clamps shown in Figure 8. The technique of gastrojejunal anastomosis by the closed method has been described in some detail at an earlier date (24). This paper proposes to deal essentially with the experiences gained in its use and the results obtained by closed anastomoses.

THE CLINICAL MATERIAL

For the purposes of this study, I propose to relate the experiences gained in 100 consecutive anastomoses which I made in the alimentary canal, embracing a period of about 7 months since March 1, 1940. The larger number of operations to be reported concern the stomach, resection being done for ulcer in 48 patients and for gastric neoplasm in 35 cases. In 14 patients, colonic resection was performed, with re-establishment of intestinal continuity. In a miscellaneous group of 3 patients, a variety of operations were performed on the small intestine.

GASTRIC RESECTION BY THE CLOSED METHOD

The chief deterrent to earlier employment and acceptance of the closed anastomosis in the stomach has been probably on two scores. The first is the alleged danger of hemorrhage.

Fig. 3. The exposure through a left subcostal incision. Ready access is had to the fundic portion of the stomach; duodenum may readily be dealt with through same incision.

Crushing of the gastric wall at the site chosen for the anastomosis, coupled with employment of the coagulating current of the surgical diathermy apparatus, has served to insure adequate hemostasis. In this group of more than 80 gastric resections there was only one instance of postoperative hemorrhage, occurring late in the convalescence. The residual stomach (resected for massive hemorrhage believed to be due to gastric ulcer but proved to be caused by carcinoma) and the stoma were negative on gastroscopic examination and the source of the bleeding was never determined. The patient has remained well. Employment of the Hofmeister plan of anastomosis, with oversewing and inversion of the oral or upper fragment of the divided gastric wall, beyond the 6 centimeters of the lower gastric margin needed for the gastrojejunal anastomosis, dispenses with the most vascular segment from which hemorrhage is likely to occur. Visible vessels on the external surface of the stomach in juxtaposition to the anastomosis are underrun with a fine needle and ligated.

The other factor, which may have deterred some from acceptance of the closed gastrojejunal anastomosis is fear lest failure to approximate the mucosa of the stomach and jejunum may be followed by untoward effects. It is to be admitted freely that a somewhat greater width of tissue is inverted by the closed method than by the open anastomosis. Yet, the approximation must be very similar to that achieved by the Connell suture, which

Fig. 4. The steps in dissection and closure of the duodenum. Employment of the "half purse strings" at the ends combined with a few Halsted mattress sutures constitutes an eminently satisfactory method of closing the duodenum. The re-attachment of the pancreatic capsule (6 a and b) affords assurance that a secure closure has been obtained. (Reproduced from *Surgery*, 1940, 8: 275.)

has been in use for 40 years in the open anastomosis. As related above, a study of the healing process in open and closed gastrojejunal anastomosis upon the experimental animal would undoubtedly supply useful information. It would appear significant, however, that gastrojejunal anastomoses with a 6 centimeter stoma with or without enteroanastomosis, function apparently quite satisfactorily. No patient operated upon by the closed method has had to be reoperated upon because of obstruction to the efferent loop.[1]

[1] Obstruction of the efferent loop has not been observed during convalescence from gastric resection, with or without entero-anastomosis. However, in one patient, Mrs. H. J., Univ. Hosp. No. 694059, periodic vomiting developed some months after operation. The patient maintained her weight quite satisfactorily. Excision (closed) of the efferent portion of the gastrojejunal stoma was done with end-to-side union between jejunum and stomach. No obstruction was found, but a small flap of mucous membrane on the jejunal side appeared to be responsible for the periodic obstruction. The patient has remained well. (See Fig. 1 for explanation of cause of this type of obstruction.)

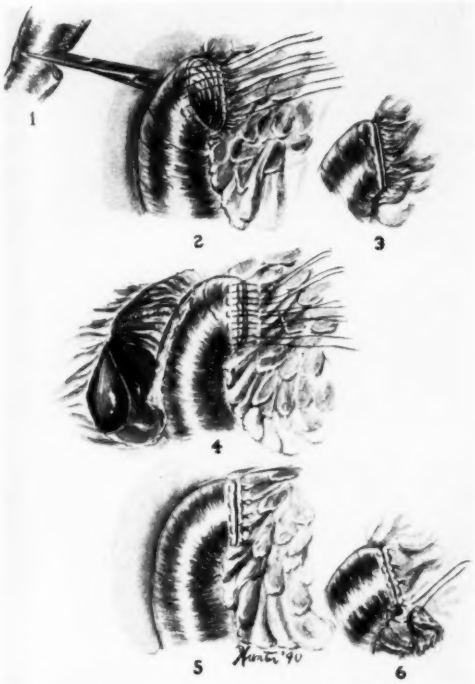


Fig. 5. The steps employed in securing satisfactory closure of the duodenum in the presence of active massive hemorrhage from a duodenal ulcer and in nonbleeding cases in which there is a posterior wall duodenal perforation. Division of the avascular ligament of the duodenum, as shown in Figure 4, brings the duodenum nearer the midline and obviates tension. This separation permits also visualization of the common bile duct (4) and affords the surgeon reliable information concerning the extent to which he may mobilize the duodenum.

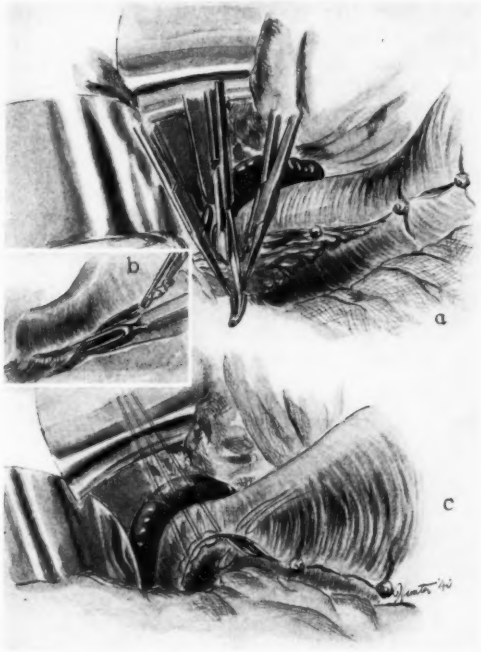


Fig. 6. Preparation of the lesser curvature. a, Ligature of the left gastric artery. b, Division of the peritoneal folds (anterior and posterior) to the esophagus. c, Closure of the peritoneal defect at the upper end of the lesser curvature by interrupted silk sutures.

A LIKELY CAUSE OF OBSTRUCTION TO THE EFFERENT OUTLET

There is a point in the anatomy of a gastrojejunal anastomosis, especially after a high gastric resection, that the surgeon will do well to contemplate. This situation is depicted in Figure 1. It is to be noted that the width of the gastric wall may be the greatest at the clamp, while the walls of the small intestine, to be approximated to the stomach, slope away from the clamp, both above and below. In the Hofmeister plan a width of not more than 4 or 5 centimeters of gastric wall may be available for the anastomosis in high gastric resections, demanding sacrifice of 85 to 95 per cent of the stomach in juxta-esophageal lesions which may be either ulcer or carcinoma. This means that unless the surgeon is wary, he may engage less of the gastric wall and more of the intestinal wall than he had in mind. In consequence, the efferent outlet, in antiperistaltic anastomoses made according to the Billroth II plan of operation, with such disparities in the lengths of the approximated segments will exhibit often definite narrowing. Through this agency, obstruction is less likely to occur at the afferent inlet in the Hofmeister antiperistaltic plan of operation, because inverted gastric wall is available for approximation without narrowing of the stoma. In my opinion, obstruction to the efferent loop, no matter whether the anastomosis is open or closed, is occasioned probably more often by the factor here described than by any other. The surgeon who employs the closed method tests always the patency of the stoma at the afferent

inlet and the efferent outlet. He knows when he has narrowed the gastric outlet. He knows too that a 9 centimeter anastomosis is no better than one 6 centimeters in length, if the efferent outlet is narrow. The surgeon who employs the open anastomosis assumes usually that the orifices of the stoma are patulous and terminates examination of his handicraft often by describing a "stoma admitting three or four fingers." The length of this opening is of *no* significance; what really matters is, how large are the *orifices* of the stoma?

DANGER OF OBSTRUCTION TO AFFERENT INLET AFTER GASTROJEJUNAL ANASTOMOSIS

Whereas there are scores of papers in the surgical literature concerning obstruction of the gastric outlet after gastric resection or gastrojejunostomy, there is scarcely any mention of the hazards of obstruction of the afferent loop. A few authors admit having observed gangrene of the retroperitoneal duodenum or the jejunum proximal to the anastomosis.

One of the best risks in the group of patients with carcinoma of the stomach died (Mr. S. S., U. H. No. 695813, aged 59 years) about 48 hours after operation with hyperthermia, the rectal temperature reaching 106 degrees Fahrenheit. Because of signs of cerebral irritation (positive Babinski and rigidity), it was believed that the patient died of a cerebral accident. Permission for autopsy was denied, but permission was granted to open the incision. The loop of jejunum proximal to the stoma was found rather dilated as was the retroperitoneal duodenum. The gut was not sectioned.

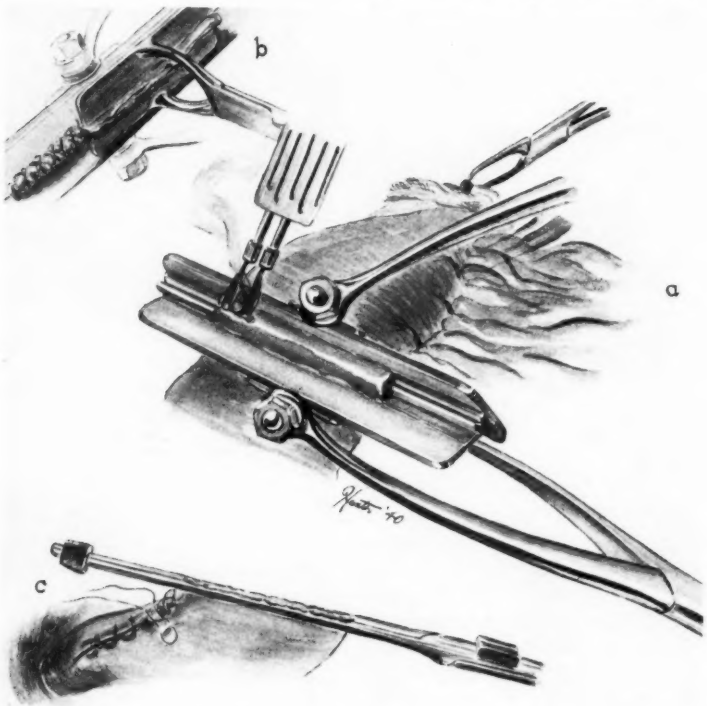


Fig. 7. Amputation of the stomach. a, Division of the stomach on the resection ledge of the lower clamp (Fig. 8). b, Closure of the upper end of the amputated stomach. The clamp engages 6 centimeters of gastric wall for the anastomosis. c, The large gastric clamp has been removed and the aseptic resection clamp has been applied in the crushed groove. The area sutured over at the upper end is inverted with a single row of interrupted mattress sutures of fine silk. The upper suture lies usually at the juncture with the esophagus.

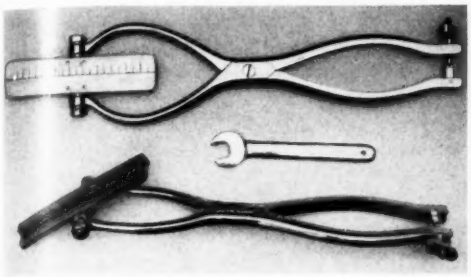


Fig. 8. Gastric clamps for the closed gastric resection. The clamp above the wrench is applied first. By loosening the burrs above and beneath the blade, the handles may be rotated into the most convenient position. The clamp below the wrench presents a resection ledge. This clamp comes away with the segment of the stomach to be removed. Figure 7 indicates how the clamps are used in the closed gastric resection.

An entero-enterostomy had been made at operation and 600 cubic centimeters of a bile stained fluid had been obtained with the inlying gastric tube in the first 24 hour period after operation. The next day 1250 cubic centimeters were obtained. The oral intake during the first 24 hour period after operation was 250 cubic centimeters and 800 cubic centimeters the second day.

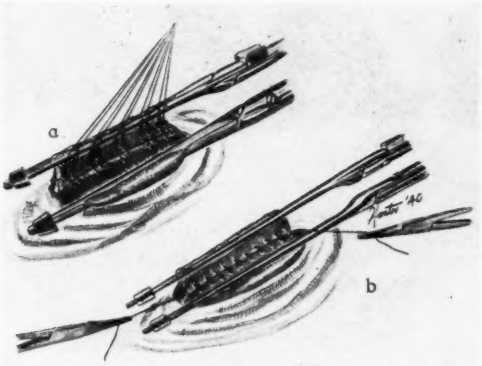


Fig. 9. The posterior portion of the gastrojejunal anastomosis. a, Placement of the first posterior row of interrupted Halsted mattress sutures. These sutures are to be placed a distance of less than 1 centimeter away from clamp. (See caption, Fig. 1.) Note position of the clamps, rotated to permit easy placement of the sutures. Five sutures are placed before any are tied. Four additional sutures are then placed between, making a total of 9 (usual number for a 6 centimeter gastrojejunal anastomosis). As each is tied, the assistant (second) who holds the clamps rotates them inward to afford maximal approximation at *the site of tie*. b, Second posterior suture (running chromic catgut No. 000). Portion of jejunum above clamp not yet removed.

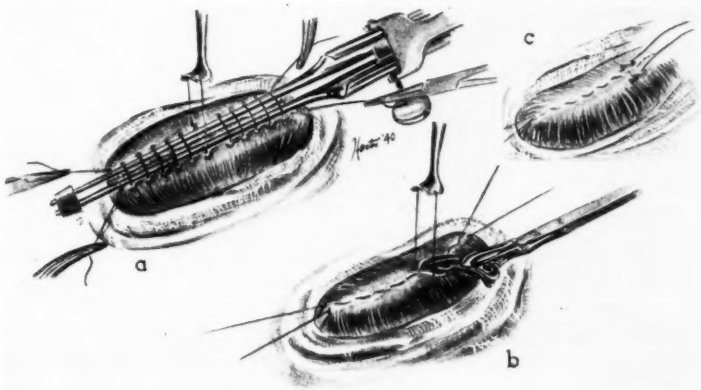


Fig. 10. The anterior portion of the anastomosis. a, The jejunum above the clamp (Fig. 9) has been cut away with the cautery—not directly on the clamp, but about 2 millimeters above the clamp. The single ferrules shown in Figure 9 have been removed, the handles of the clamps have been rotated, the double ferrule has been applied, engaging the tips of both clamps and the approximation device over the handles is in place. b, The running catgut suture shown in *a* is pulled upon after removal of the clamps. Elevation of the mid portion of the suture on an eyelid retractor permits aspiration of the residual gastric pouch with a sucker, after which the forked catheter is pulled out with an alligator type of forceps. A fork of the catheter is placed carefully into each jejunal limb of the anastomosis. c, After the forks of the catheter are in place, the anterior catgut suture at each end is tied to the posterior running catgut suture. Before these ends are tied, a fine silk suture is placed at each end, to prevent buckling or a "purse string effect" when the anterior and posterior sutures are tied.

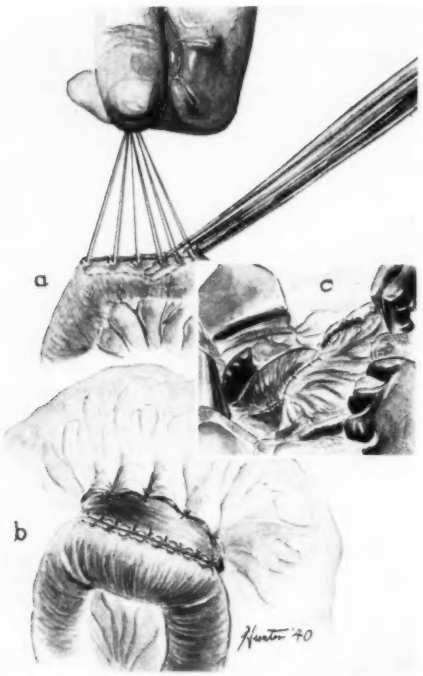


Fig. 11. a, Method of removing clamps in the anterior portion of the anastomosis. The tips of the clamps are depressed. The interrupted silk suture is shown here. b, The completed anastomosis below the transverse mesocolon. A single row of interrupted Halsted mattress sutures of fine silk completes the anastomosis. Three or 4 sutures serve to anchor the mesocolon to the gastric wall. No anchoring sutures are placed in the jejunum. c, The residual gastric pouch seen from above the mesocolon.

On two occasions, at an earlier date, this same situation had been observed without obvious gangrene of the bowel. Both patients were exceedingly poor risks because of long standing obstruction. One of the patients had also a far advanced tuberculosis. Inasmuch as the histologic sections from the retroperitoneal duodenum or jejunum proximal to the stoma failed in both instances to show any evidence of tissue change, the local distention was explained away as being "paralytic" in origin. The surgeon was exonerated from blame and the cause of death was ascribed to the general debility of the patient.

In the instance of the patient referred to above, however, the stigma of protracted preoperative obstruction was absent. It appeared that slight rotation of the proximal afferent loop high on the lesser curvature may have kinked the bowel, the entero-anastomosis constituting the only source for the escape of the duodenal contents into the stomach. Mindful of the observations of C. A. Dragstedt and his associates with reference to the effect of relatively low intraluminal pressures upon preventing the return flow of blood from the duodenum, it was reasoned that the most likely cause of death in the patient referred to above was a closed-loop duodenal obstruction.

Together with my colleagues Drs. Lyle Hay and David Lynn, a somewhat similar situation was established in dogs by dividing the pylorus and obstructing the jejunum a short distance beyond the duodenojejunal angle. Death from hyperthermia was almost a uniform finding. The intraluminal pressure in the obstructed duodenum was found to vary between 20 and 45 centimeters of water pressure in the dogs.

These observations will be reported in greater detail at a later date. Suffice it here to say, that since the occurrence referred to above took place, I have used a forked catheter with a tube in both the ascending and descending limbs of the anastomosis, without entero-anastomosis (Fig. 2). When entero-anastomosis is employed in carcinoma (but I am omitting it regularly now since using the forked inlying duodenal tube), the catheter is pulled down the efferent loop through the entero-anastomosis by means of a long alligator type of forceps with a blunt nose, and the tip of the tube is placed well into the ascending limb of the stoma. I have now used the forked catheter without entero-anastomosis in a large number of gastric resections, including several virtual subtotal excisions for juxta-esophageal lesions in which 85 to 95 per cent of the stomach has been sacrificed. It is possible that mere placement of a straight tube through the gastrojejunal anastomosis into the proximal afferent loop would achieve the same purpose. Proper placement of a division of the forked catheter into the afferent loop is undoubtedly the more important consideration. Yet, I feel a little more secure that the stoma will function satisfactorily on withdrawal of the tube 72 hours after operation

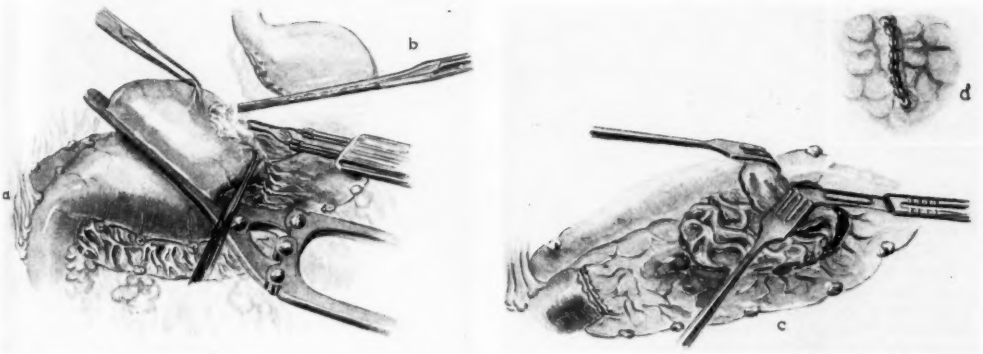


Fig. 12. Method of dealing with a carcinoma of the stomach intimately adherent to the pancreas over a wide area. a, The stomach is severed above the lesion. After aspiration of the distal gastric pouch with a sucker, the posterior gastric wall is cut through with the cautery leaving the adherent tumor on the pancreas. b, The upper residual gastric pouch. c, The residual tumor is shaved away together with a thin layer of pancreas. d, Closure of the defect in the pancreas (transverse) with interrupted mattress sutures.

when the forked tube has been in both afferent and efferent loops of the anastomosis.

It appears somewhat strange that this factor of obstruction of the afferent loop should have received no discussion in the complications of gastrojejunal anastomoses. I have the impression that it has loomed larger in the item of mortality after gastric resection than is apparent. Patients who succumb from hyperthermia with "pneumonia or atelectasis" 36 to 72 hours after gastric resection should be examined critically with this consideration in mind. Among the 4 deaths in the 100 consecutive cases reported herewith, pneumonia or atelectasis was not the primary cause of death in any instance.

THE INDICATIONS FOR GASTRIC RESECTION

The two usual conditions for which one performs gastric resection are ulcer and neoplasm. In the latter, sacrifice of a good portion of the stomach is obligatory if the tumor, whether carcinoma, lymphosarcoma, leiomyoma or polyp, is to be gotten rid of. In ulcer, and especially in duodenal ulcer, gastric resection is an indirect attack on the ulcer diathesis, achieving its end by effectual reduction in gastric acidity, which attends regularly extensive resection and gastrojejunal anastomosis. Gastrojejunostomy and other anastomotic procedures are not physiologic operations for ulcer, in that they fail to reduce gastric acidity and leave too much to chance as evidenced by the high incidence of recurrent or stomal ulcers.

PRE-OPERATIVE PREPARATION FOR GASTRIC RESECTION

There are certain fundamental requisites which must be met by all patients submitting themselves for major abdominal operative procedures. They are especially mandatory in gastric surgery. Patients must reach the operating table with the stomach empty. This objective is achieved most readily by placement of an indwelling duodenal tube into the stomach to which suction is applied for an hour prior to operation, throughout the operative procedure, and for about 72 hours after operation. In patients exhibiting high grade pyloric obstruction, a large gastric tube is employed for washing the stomach prior to insertion of the duodenal tube. Even despite this ritual, in 3 or 4 of the carcinomas in this group, there was still considerable material left in the stomach at operation. Vegetables eaten last by the patient a few weeks previously, in carcinomas with high grade obstruction have been removed through a gastrostomy opening at operation, immediately prior to undertaking the resection. In large polypoid bleeding tumors, it may be necessary similarly to aspirate the intragastric hematoma resulting from manipulation of the stomach before

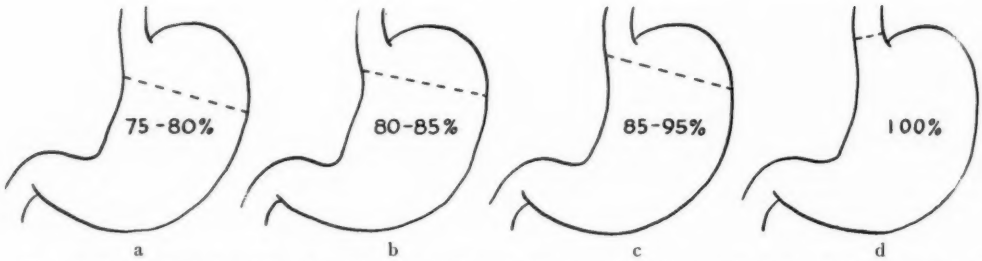


Fig. 13. Usual extent of excision of gastric tissue in the Hofmeister-Pólya procedure. a, In ulcer, excision of 75 to 80 per cent of the stomach with gastrojejunal anastomosis is necessary to insure achlorhydria. b, In carcinoma, even if the lesion is in the antrum, sacrifice of the entire lesser curvature is necessary to afford assurance that the disease in the stomach has been eradicated. c, In juxta-esophageal lesions, no matter whether ulcer or carcinoma, subtotal sacrifice (85 to 95 per cent) of the stomach becomes necessary. The nature of the lesion present frequently is not definitely known until the lesion has been excised. d, Total gastrectomy.

the anastomosis is made. It is decidedly unsafe to leave the hematoma in the tiny residual gastric pouch, lest it be regurgitated into the trachea during recovery from the anesthetic. Keeping the stomach constantly empty during the induction of the anesthesia, throughout the operation, and during the early convalescence is the best assurance against pneumonia. Aspiration into the trachea is probably the most important cause of pneumonia in surgical patients. Pathologists have directed attention recently also to this occurrence.

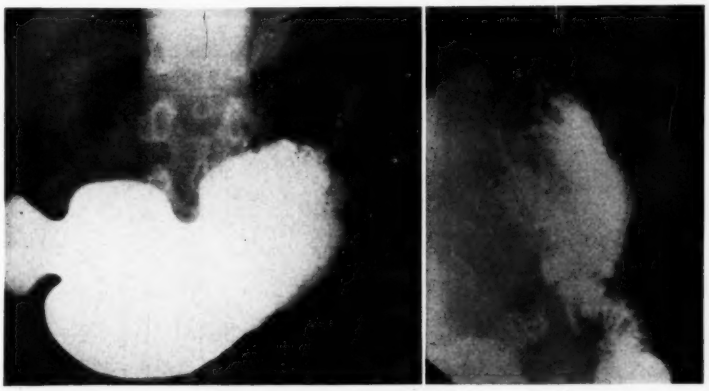
The nutritional status of the patient should be satisfactory. In patients who are practically totally obstructed, this requirement may be extraordinarily difficult or impossible to meet fully. Yet, I have the impression that the necessity for the staged procedure, that is, a preliminary jejunostomy or gastrojejunostomy, is largely a matter of past history. Unless a patient presents most unusual emaciation he can be prepared ordinarily for a one stage gastric resection by para-oral feeding supplemented by whatever fluid can be passed through the stenotic pylorus. No preliminary gastric drainage operations have been performed in this series of patients. None of the patients were refused gastric resection because of the presence of an obstruction in the pylorus.

The usual plan of procedure in obstructed cases is to supply nitrogen by giving human plasma in 500 to 600 cubic centimeter amounts, half the quantity being given twice daily intravenously.[1] This amount of protein will maintain the patient in satisfactory nitrogen equilibrium. My colleagues (26) and I have recorded in a preliminary communication elsewhere our experience with the intravenous administration of bovine plasma as a substitute for human blood or plasma in the treatment of contraction of protein stores or blood volume reductions. An enlarged experience suggests that this agency may come eventually to play an important rôle as a hospital procedure in the care of patients. The caloric requirement must be met by the slow intravenous administration of 10 per cent glucose solution (1000 to 1500 cubic centimeters).[2] Not infrequently, however, feeding by a Murphy drip into the stomach of boiled milk to which lactose has been added (100 grams of lactose to 1 liter of milk) can be accomplished even though oral ingestion of 2 to 3 ounces at a time may be accompanied by vomiting or high grade retention. Another solution which affords a satisfactory means of supplying calories (carbohydrate) and protein is a mixture of 40 grams of casein and 200 grams of lactose in a liter of 0.45 saline solution.

Satisfactory water and salt balance are determined best by giving enough fluid to insure a urine output of 800 to 1000 cubic centimeters

[1] Fortified amino-acids for intravenous use, which will maintain patients in satisfactory nitrogen equilibrium will come eventually to supplant plasma for this same purpose.

[2] Latterly, we have been giving 1500 cubic centimeters of a 20 per cent glucose solution intravenously through a 22 gauge needle placed in one of the small veins of the forearm. Surprisingly little sugar (less than 1 per cent) appears in the urine, when the fluid is given slowly. The patient may move his arms freely during the long interval of administration



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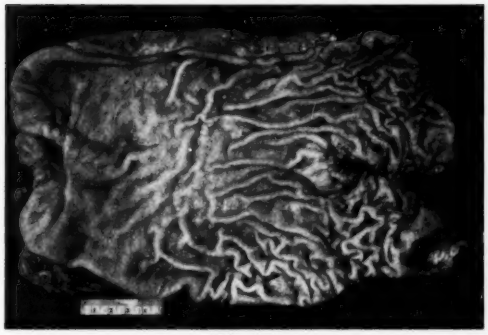


Fig. 14c.

Fig. 14. Gastric resection for posterior wall duodenal ulcer. a, The large dilated, obstructed stomach before operation. b, Residual gastric pouch after operation. c, The excised portion of the stomach (75 per cent). The ulcer is shown distal to the unrugated antrum. The rugations of the corpus and fundus are marked by contrast. The area of the excised specimen was 480 square centimeters. (Type a resection as shown in Fig. 13.)

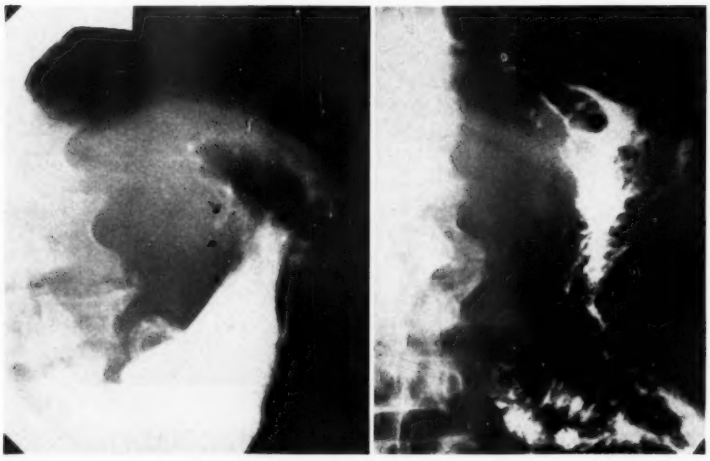
a day in which 2 to 3 grams of sodium chloride is excreted. These are probably the most reliable tests of satisfactory hydration and chlorination. Occasional plasma chloride determinations serve as a satisfactory check against the development of hypochloremia. Careful weighing of patients immediately before operation and each morning for the early convalescent period after operation on a bedside scale helps to orient the staff in ascertaining the status of hydration of the patient (Fig. 18). In patients with low cardiac reserve this expedient is most helpful after operation in determining the requirement of water.

Vitamins B_1, C, and nicotinic acid are supplied in daily doses of 10, 50, and 100 milligrams hypodermically, respectively, for a few days prior to operation, and through a good portion of the postoperative period. Patients with both ulcer and carcinoma have observed dietary restrictions usually and have taken, often in consequence, an inadequate amount of vitamins.

Anemic patients must be transfused with whole blood. In a few patients in this series, we were unable to get the hemoglobin above 50 per cent despite repeated transfusions because of persistent blood loss from an ulcerating carcinoma. Patients exhibiting shock from massive hemorrhage must have restoration of a contracted blood volume by transfusion before operation is undertaken.

SELECTION OF PATIENTS FOR OPERATION

Ulcer. In this clinic, the attitude of both internists and surgeons to the ulcer problem has been, in the main, one of great conservatism. A large number of patients presenting satisfactory indications for operation have, therefore, been accumulating in our outpatient



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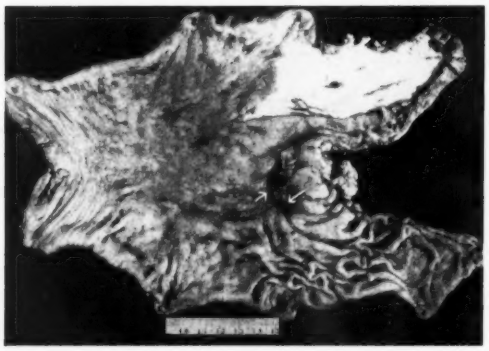


Fig. 15c.

Fig. 15. Subtotal resection for a juxta-esophageal lesion believed to be carcinoma, but found on microscopic examination to be a benign ulcer. a, The large juxta-esophageal lesion on the lesser curvature. b, The tiny residual gastric pouch after sacrifice of 95 per cent of the stomach (Fig. 13, Type c resection). c, The excised stomach. The arrows indicate the site of the ulcer. The mucosal rugations are not prominent, even in the fundic position as contrasted with Figure 14 c. The stomach being considerably smaller than that shown in Figure 14 a, and even though 95 per cent of the stomach was sacrificed, the area of the excised specimen was only 297 square centimeters.

clinics for years. Of the 48 ulcers in this series, a fairly large number had had antecedent perforation or hemorrhage. Six patients (5 ulcers and 1 carcinoma) were operated upon during active massive hemorrhage. One boy of 14 admitted 5 times for acute massive hemorrhage was submitted to extensive gastric resection. Six patients in the group had gastrojejunal ulcer following an antecedent gastrojejunostomy. One of these had also a pyloric carcinoma and is placed, therefore, in the carcinoma group.

Malignancy. Obviously inoperable cases are turned away in the medical outpatient clinic. I am in no position to say, therefore, what proportion of patients in whom the diagnosis of gastric malignancy was made come ultimately to gastric resection. Of the patients admitted to the surgical wards, all were explored but 1. This patient, though exhibiting an apparently operable lesion, was found to have supraclavicular and pulmonary metastases. Six patients were explored but not resected. For 1 of these I had done an extensive gastric resection 4 years previously for carcinoma. On re-exploration, metastases were found in the liver. Another had a carcinoma involving both the lower esophagus and stomach and may not properly be considered, therefore, to be a primary gastric neoplasm. Of the remaining 4, on whom exploration was carried out, 2 exhibited total

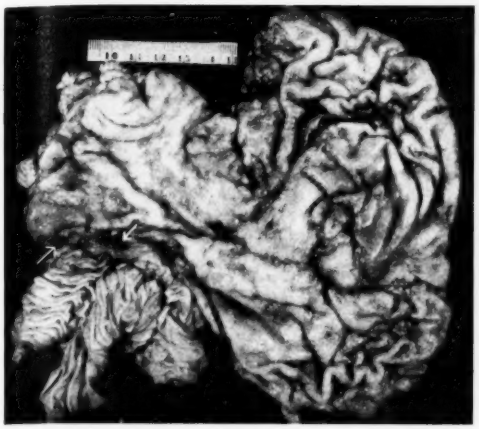


Fig. 16. Emergency gastric resection for a bleeding gastrojejunal ulcer. The patient was 57 years of age and the gastrojejunostomy had been done 20 years before. Ten thousand cubic centimeters of blood was given prior to and during the operation. The operation was done in steep Trendelenburg position because of the difficulty in sustaining a stable blood pressure. The arrows indicate the ulcerations in the stoma. The area of the excised gastric tissue was 301 square centimeters.

gastric involvement and extensions unfavorable for an operative procedure commanding the risk of total gastrectomy. The 2 remaining patients exhibited carcinosis of the peritoneum and were rejected for even palliative partial resection. The resection rate in the patients explored for malignancy was 88.5 per

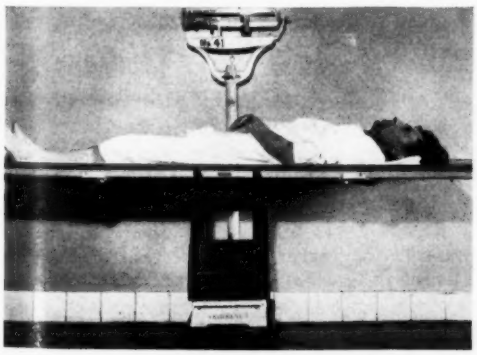


Fig. 18. Manner of obtaining bedside weights of patients after operation. The block on the scale supports the stretcher. Significant gains or losses in weight may be detected readily. The weighing of patients before and after operation should come to be an important item in determining the status of hydration.

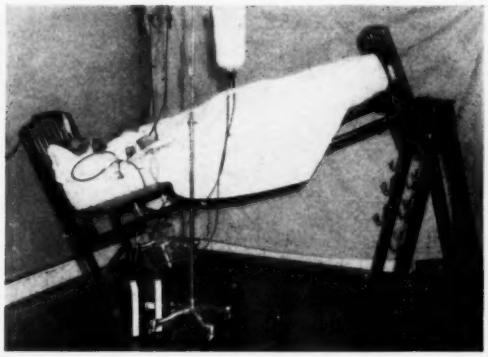


Fig. 17. Shock frame employed routinely after major operative procedures performed under inhalation anesthesia. Placement of the patient in steep Trendelenburg position obviates aspiration of mucus or gastric content into the trachea while the patient is asleep. The nasopharynx is kept dry by intermittent suction. The shock frame is of value also in supporting the blood pressure.

cent (31 out of 35 cases). No gastrojejunostomies were done for malignancy. The only gastrojejunostomy in this group of 100 patients was done for a patient with congenital cystic disease of the liver in which the liver cysts obstructed the pylorus.

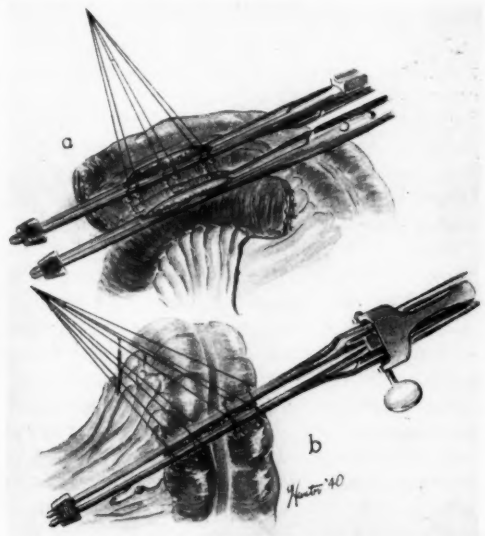


Fig. 19. Closed anastomosis in the colon. a, Lateral anastomosis between the ileum and transverse colon after removal of a malignant tumor in the right half of the colon. b, Oblique end-to-end anastomosis in the pelvic colon.

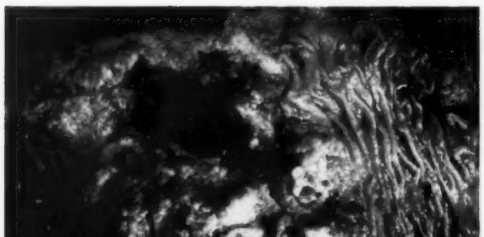


Fig. 20. Huge carcinoma of the cecum. a, left, A large necrotic ulcer is shown on the base of the cecum.

b, Perforation of the carcinoma onto an adjacent loop of small intestine.

Resection was carried out as a palliative measure in 2 patients exhibiting liver metastases. Adherence of the tumor to the pancreas or the transverse mesocolon was not considered as a contra-indication to operation, nor was extensive local lymph node involvement. In 1 case, however, an attempt to carry too far a difficult palliative resection in a man of 72, exhibiting a large periduodenal lymph node mass intimately adherent to the duodenal wall, eventuated in an insecure closure of the duodenum with resultant duodenal fistula from which the patient died 13 days after operation.

Nineteen, or slightly more than half of the resection group for gastric neoplasm, were over 60 years of age. Seven were 70 or over.

Gastric polyps. In the medical clinic, all patients exhibiting gastric symptoms with negative x-ray findings are submitted to gastroscopic examination. Polyps are found not uncommonly in such patients. In the majority, we have awaited roentgenographic confirmation of their presence before submitting the patients to operation. There are 3 patients in this series, upon whom gastric resection was done for benign polyps. One of these was a man of 74 with jaundice from common duct obstruction. Four stones were removed from the common bile duct and the stomach was resected. The large gastric polyp which was believed to be malignant was found to be benign. The convalescence was uneventful.

THE OPERATION

All operations in the series were carried out under inhalation anesthesia. Cyclopropane, reinforced occasionally by ether, was the anesthetic agent in all cases. All the gastric resections save those for massive hemorrhage were carried out through a left subcostal incision. An unusually satisfactory exposure of the entire lesser curvature and gastric fundus may be obtained through this incision. It is distinctly superior to a right or left rectus incision in affording access to the upper portion of the stomach. The character of the exposure obtained is indicated in Figure 3. At the same time, the duodenum may be dealt with readily through the same incision. Its disadvantage, as contrasted with the vertical incision, is that it takes a little longer to make and still longer to close, since the interrupted silk suture method is used. Evisceration has not as yet been observed with this type of incision.

TECHNIQUE OF GASTRIC RESECTION

The details of establishing the gastrojejunal anastomosis after gastric resection have been described previously. The variants in technique that have been adopted in the metamorphosis of the operation are not many and were alluded to briefly in an early part of this paper. The larger number of the gastric patients in the series, including all the neoplasms and the majority of the ulcers, were operated upon according to the Billroth II plan of operation, pylorus, antrum, and an extensive portion of the stomach being removed. Intestinal continuity was obtained invariably by the Hofmeister plan of retrocolic, inferior, terminolateral anastomosis (Fig. 7). Ent·ro-

anastomosis was performed in all the carcinomas in the earlier part of the series and in a number of the resections for ulcer. With development of the forked catheter (Fig. 2) to obviate stasis in the proximal jejunal loop, entero-anastomosis has been abandoned.

The greater omentum is excised regularly in gastric resection for malignancy. The pylorus and a good portion of the duodenal wall are then freed up by dissecting the medial or posterior duodenal wall free from the pancreas. The duodenum is divided with the Petz suturing apparatus, the crushed wall between the two rows of clips being cut with the cautery. The duodenum is inverted by the technique described previously. In 9 patients among the 48 ulcer resections, the duodenum was opened during the course of the dissection because of the presence of a posterior wall perforation. This is the invariable occurrence in operations undertaken during the course of active massive hemorrhage from a duodenal ulcer. The technique described previously constitutes a satisfactory means of closing the duodenum (25). I have had no experience with the pyloroplastic procedures described for dealing with this type of ulcer (Steinberg). As has previously been indicated, the consistent attainment of achlorhydria to histamine stimulation necessitates sacrifice of 75 to 80 per cent of the stomach. Because of the great tendency of gastric carcinoma to spread in the mucosa and submucosa (Verbrugghen), I make it a regular practice, even in lesions limited to the antral zone, to excise practically the entire lesser curvature amputating the stomach from 1 to 2 centimeters distal to the esophagus on the lesser curvature. On the greater curvature, a greater length of gastric wall is left. Inasmuch as the only principal source of blood supply remaining to the small residual gastric segment, after this type of excision, comes from one or two of the vasa brevia of the splenic artery, it is very important to save the splenic artery, as well as these small branches. The usual upper sites of resection are indicated in Figure 13.

There was only 1 total gastric resection in the group. Only 2 have been done in the past year and both patients are well.[1] A number of

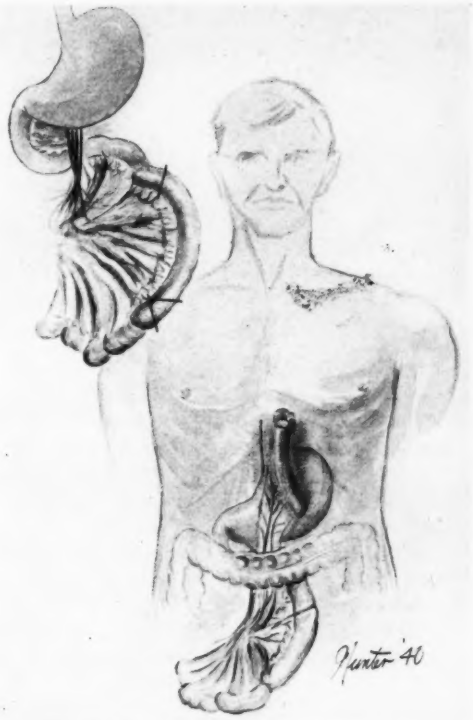
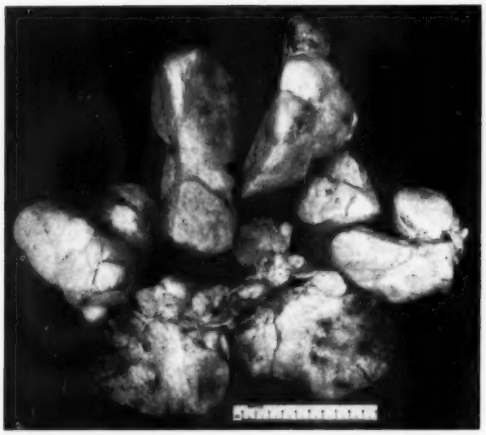


Fig. 21. Schematic representation of gastrojejunoplasty (Wullstein-Roux) as a feeding tube for carcinoma of the esophagus. A segment of the upper jejunum is isolated, the continuity of the small intestine being re-established by oblique end-to-end anastomosis. An oblique end-to-side anastomosis is made between the aboral end of the isolated jejunal segment and the stomach. The oral end of the jejunum is brought out upon the thoracic wall to as high a level as the mesentery permits. Maintenance of the patient in a steep Trendelenburg position encourages migration of the small intestine to the upper abdomen and lessens tension upon the mesentery of the isolated jejunal loop.

virtual subtotal resections ranging from 85 to 95 per cent have been done, in which the lesser curvature was excised completely, either for juxta-esophageal ulcer or for carcinoma extending the entire length of the lesser curvature. The left subcostal incision and the Hofmeister plan of operation permit the anastomosis to be accomplished without difficulty. The success of the procedure depends in large measure on leaving at least one of the vasa brevia from the splenic artery intact.

[1] One additional total gastrectomy for leiomyosarcoma has been done since this paper was written. The patient did well.



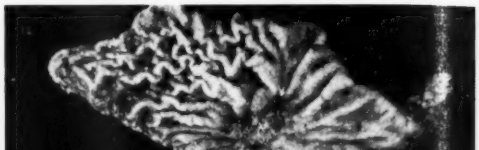


Fig. 22. Gastric resection for Krukenberg tumor of the ovaries and uterus. a, left, The pelvic metastases excised at the first operation. The abdomen was the size of a 6 months' pregnancy (see text). The excised tissue weighed 335 grams. It is to be noted the scale of projection is only one-half of b. b, The excised stomach, showing the superficial carcinomatous ulcer on the lesser curvature. Microscopic study of the stomach demonstrated that the tumor had spread widely in the mucosa and submucosa. The upper area of gastric resection was beyond the microscopic spread of the tumor, however.

For several months, I have been employing the type of clamp depicted in Figure 8, instead of the usual Payr or the large gastric crusher, employed initially. The virtue of these clamps lies in this, that the clamp can be applied from the right side. After it is fixed in place, the handles may be rotated by loosening the nut on the upper and lower blades. The likelihood of tearing the few remaining gastric vessels near the spleen is considerably less than with the use of the straight clamp. Further, this new clamp[1] is especially adaptable for use in the left subcostal incision.

The illustrations made for me by Mr. Herbert Hunter indicate nicely the various steps in the procedure (Figs. 3 to 12). A special clamp 6 centimeters in length (Fig. 7b) insures engagement of the proper length of tissues for the gastrojejunal anastomosis. The method of dealing with the forked catheter is shown in Figures 2 and 10b. On completion of the anastomosis, the defect in the transverse mesocolon is closed by placing three sutures in the anterior gastric wall, about 1 centimeter behind the suture line. The incision in the abdominal wall is closed with interrupted sutures of fine silk. No drainage is instituted.

[1]The clamps and forked gastric catheter may be obtained through V. C. Mueller Company, Chicago, Illinois.

POSTOPERATIVE CARE

Position. The patient is maintained in moderately steep Trendelenburg position during the recovery period until he is fully awake (Fig. 17). Great care is observed to make certain that the indwelling tube is keeping the stomach empty. The nasopharynx and trachea are kept free from mucus by frequent aspiration with an electric suction apparatus until the patient is fully awake. After the patient is fully awake he may take sips of water by mouth, and the elevation of the foot of the bed on the shock frame is decreased gradually. Slight elevation of the foot of the bed is maintained, however, well into convalescence, until the patient becomes quite active. Resumption of a steep grade of the Trendelenburg position is employed only for drops in arterial blood pressure.

Vigorous movement of the extremities is enjoined upon the patient from the very first day after operation. Nurses, internes, house-officers, and staff admonish the patient "to move his arms and legs a thousand times a day." I have the feeling that use of the Trendelenburg position and active motion are important items in thwarting pulmonary embolism.

Fluid administration. The fluid requirements of surgical patients have been very well

defined by Coller and Maddock and their associates. The careful notation and daily summary of the fluid administered, its amount and character, the fluid aspirated from the stomach, the amount of the urine and its sodium chloride content on the face sheets of the temperature record constitute a guide of the greatest importance in helping to orient the surgeon in the fluid and electrolyte balance of the patient. In a straightforward case, 3000 to 4500 cubic centimeters of fluid is given postoperatively each day for the first 2 or 3 days—sufficient to insure a urine output of about 700 cubic centimeters daily. Of this amount 500 to 1000 cubic centimeters is normal saline solution (4.5 to 9 grams of sodium chloride). The profound effect of prolonged operation and anesthesia upon the loss of fluid through the skin by sweating must be taken into account in the giving of fluid. Despite apparently generous administration of fluid, a lag in urinary excretion not uncommonly follows operation for a few days. As a matter of fact, some of our patients excrete only 300 to 500 cubic centimeters of urine of low specific gravity daily for the first 2 days. The ordinary surgical risk may be given fluid liberally (4500 to 5000 cubic centimeters daily) to increase the output of urine in the early postoperative period, but, as will be pointed out presently, this may prove a hazardous procedure in patients who are poor risks. Inspection of records indicate that 25 to 35 grams is the usual intake of sodium chloride as saline solution during the convalescent period. Many surgeons give far too much salt and invite pulmonary and general tissue edema in consequence.

We have erred occasionally on the other side and have not given enough sodium chloride to replace adequately that lost by sweating and that aspirated from the stomach (sodium chloride value of sweat estimated at 3 grams per liter and 5 grams per liter for gastric aspirations). The deficiency is suggested when the excretion of sodium chloride falls to less than a gram per day. Occasionally it is heralded by somnolence without obvious cause. It is startling to note how the administration of sodium chloride brightens and awakens such patients out of their drowsy lethargy. An occasional plasma chloride determination serves to orient the staff correctly in appraising such situations.

BEDSIDE WEIGHING OF PATIENTS AFTER OPERATION

In old and feeble patients with impaired cardiac reserve, the orientation value afforded by frequent determination of the patient's weight cannot be overemphasized as a useful guide in determining the state of hydration. Weighing of the patient at the bedside will come to be undoubtedly a routine measure in ascertaining the fluid requirements of poor risk patients, whose margin of latitude for the tolerance of increases of plasma and extracellular fluid volume is very small. I have come to feel that the bedside weighing of such patients is an indispensable measure (Fig. 18). As a matter of fact, it is a good plan to ascertain pre-operatively the weight of all patients prior to major surgery. The loss of water by vaporization is so variable a factor that only the weighing scale can be depended upon for orientation in the patient whose capillary permeability, cardiac or renal reserve border on decompensation.

The lag in urinary excretion following operation is a variable factor. When a fairly liberal quantity of fluid has been given postoperatively and oliguria (daily urinary excretions of only 200 to 350 cubic centimeters) persists, it may be extremely hazardous to attempt to provoke diuresis by giving larger quantities of fluid by vein or under the skin. This lag in urine excretion is an interesting and perplexing phenomenon and deserves the serious attention of surgeons.

Weighing within 100 grams of absolute accuracy may be achieved readily. The confusion in the surgeon's mind with reference to the status of hydration in poor risks does not concern grams but weight disparities of 2 to 5 kilograms and more. Only he who has made these observations knows how disoriented he may become in reference to the status of hydration of his patient. Most of these errors concern the overadministration of water to patients with poor cardiac function. The heart may be well compensated before operation, but with the increase of plasma and

extracellular fluid volume which attends the too liberal administration of water, compensation breaks.[1]

Inasmuch as a large number of these patients are in the upper age brackets and a number present evidence of cardiac damage, we have reverted largely to the subcutaneous administration of fluid. Intravenous administration of fluid accelerates the heart rate, not uncommonly and now and then a patient complains of pain over his heart if the fluid goes in too rapidly. Blood, plasma, and high concentration of glucose (10 or 20 per cent) must, of course, be given intravenously.

Shock. The best treatment for shock is avoidance of blood loss. The operation is carried out in slight Trendelenburg position, the plane of the feet being a few inches higher than the head. This measure helps to support a stable blood pressure. A solution of 5 per cent glucose in distilled water is given subcutaneously during the operation, quantities of 1000 to 1500 cubic centimeters being absorbed during the course of a 3 to 4 hour operation. A small needle is placed in one of the ankle veins through which saline solution, not exceeding 500 cubic centimeters in amount, is given. If the blood pressure tends to fall or the pulse accelerates, a transfusion of 500 cubic centimeters of citrated blood, or more if necessary, is given. The shock frame shown in Figure 17 is an important item in supporting the blood pressure after operation. On return of the patient to the ward, the nurse in attendance checks the blood pressure frequently during the early convalescent hours.

The bladder. So large a percentage of patients cannot void after these operations that I have come to insert an indwelling urethral catheter as a matter of routine. This practice helps also in determining accurately the daily urine output during the early convalescence. The subcutaneous administration of 1 to 2 grams of sulfanilamide avoids the occurrence of pyelonephritis.

The inlying duodenal tube. Suction is kept up continuously until the forked catheter is removed 72 hours after operation. The patient takes water and other clear fluids by mouth as soon as awake. After the tube is removed, the diet is increased gradually, but patients are offered fluid and semisolid food in small amounts throughout the day, until they can cough without pain. After that (about the sixth day) there is little likelihood of regurgitation of food into the trachea. When the patients leave the hospital, they are instructed to take a well balanced diet. Ulcer patients are urged to eat meat again and they welcome the opportunity. Inasmuch as achlorhydria is the objective of the surgeon when operating for ulcer, no dietary restrictions need be imposed on these patients.

Pneumonia. The incidence of pneumonia in this group has been surprisingly small, and the few pneumonias which were observed were largely benign. However, it would be a serious omission did I fail to indicate the great protective value afforded by the intravenous use of sodium sulfathiazol or sodium sulfapyridine. Dr. Wesley Spink of the medical service, who has been keenly interested in the chemotherapy of surgical infections supervised kindly the treatment of the pneumonias. The usual dose of sodium sulfathiazol was 2 grams intravenously initially, an additional gram or two being given every 4 to 6 hours. A daily dose of 6 to 8 grams was not exceeded.

In the older age group of patients (70 and over) I have come to substitute sodium sulfathiazol or sodium sulfapyridine for sulfanilamide in the prevention of urinary tract infection attending the temporary use of an indwelling catheter, feeling that the drug may at the same time exercise a beneficial influence in thwarting pneumonia.

COLON RESECTIONS

The exteriorization operation of Bloch, Paul, and Mikulicz constituted for years the preferred method of dealing with a large number of the malignancies in the colon. The relative safety of resection with primary anastomosis, whether in the right or left colon has come, I believe, to supplant largely the exteriorization operation. Complete excision of metastases in lymph nodes in the mesentery can be carried out far better with the primary resection, and local recurrence is certainly less frequent than

[1] In a patient weighing 50 kilograms, a postoperative weight gain of 3 kilograms represents 6 per cent of the body weight, but 10 per cent of the body water (water constituting 65 per cent of body weight). It is obvious, therefore, that postoperative gains in weight must be watched in the poor risk patient with *scrupulous* care.

with the exteriorization operation. My associate, Dr. Orwood Campbell, has for some time been an advocate of primary excision. Surgeons have been somewhat reluctant to give up the antecedent or complementary cecostomy or colostomy for left sided resections. In the earlier cases, I chose to establish, in unobstructed lesions of the left side, a simultaneous appendicostomy or cecostomy at the time of the resection. Latterly, following Campbell's example, I do not hesitate to perform resection of either the right or the left colon without a complemental external drainage vent. All patients, of course, have an indwelling duodenal tube, suction being maintained for 4 or 5 days. Whipple believes employment of the Miller-Abbott type of tube offers an important advantage and considers it to be, in his hands, an important factor in the reduction of mortality in primary resection of the colon. Our experience has been that suction, applied to an ordinary indwelling tube *from the beginning*, will preclude the occurrence of distention. In the 14 cases reported here, the only death occurred in a lesion in which perforation had occurred, occasioning contamination in the excision of the lesion.[1]

In acutely obstructed colonic malignancies, a preliminary drainage operation must of necessity be done. Not infrequently patients with mild obstructive symptoms may be tided over by a starvation regimen (clear fluids and suction applied to an indwelling duodenal tube) and operated upon as though obstruction were not present. With reference to acute obstructions of the colon with great distention, I feel it important to reiterate here the great value of the roentgenogram in ascertaining the point of obstruction and in determining the site to be selected for decompression. Cecostomy is to be avoided wherever possible, for it is not feasible to make readily an aseptic decompression on a very tense and distended cecum. On the contrary, decompression can be established in the transverse colon with ease and far greater safety to the patient.

In the colon resection group (14 patients) there were 10 right sided lesions and 4 left sided lesions. Resection was performed in 1 instance in the presence of hepatic metastases. In 1 of the right sided lesions (perforated) a simultaneous partial excision of the circumference of the pelvic colon had to be made because of involvement by direct extension from the cecum. The continuity of the pelvic colon after the wedge excision was established by end-to-end suture. No external drainage vent was established. The operation was undertaken for supposed malignancy. The pathological diagnosis (gross) on the excised specimen was benign. The histologic diagnosis, however, confirmed the clinical impression of malignancy. Prior to operation, the mass had been believed to be outside the colon and the resection of right and left colon was done without preliminary cleansing of the colon. In the instance of a recurrent left sided lesion for which a previous excision had been undertaken elsewhere, the colostomy, which was involved by tumor, as well as the uterus was excised with primary establishment of intestinal continuity by end-to-end union. Two of the 14 patients exhibited benign lesions.

Pre-operative preparation for resection. The unobstructed patient is allowed only clear fluids by mouth for 3 days prior to operation. Three to 4 ounces of mineral oil are given daily during this time and the colon is washed out with liberal quantities of water twice daily. Nitrogen equilibrium is maintained by the intravenous administration of 500 cubic centimeters of human plasma daily. Caloric balance is approximated by the liberal administration of glucose solutions to supplement the oral intake. The water and salt balance are followed carefully even preoperatively, as outlined above under the preparation of gastric cases for operation. I have had no experience with pre-operative peritoneal vaccination. The experience of this clinic suggests that, in the absence of a perforated lesion, a well performed closed anastomosis is the best protection against peritonitis.

Anastomosis. Partial colectomies are done through a vertical, right or left rectus incision depending on the location of the lesion, or through an oblique incision crossing the midline either above or below the umbilicus. In

[1] Four additional primary colonic resections have been done since the time of this report, without mortality.

the right colon, side-to-side anastomosis between the ileum and the transverse colon is carried out usually (Fig. 19a). Occasionally,[1] an oblique end-to-side anastomosis is done. Ordinarily, 2 to 3 feet of the terminal ileum are sacrificed, with the cecum, ascending colon, hepatic flexure, and proximal transverse colon, making possible a more liberal excision of the lymph drainage area. Further, the terminal few feet of the ileum exhibit often a narrower lumen than more proximal reaches. For lesions in the transverse, splenic, descending, and pelvic portions of the colon, an oblique end-to-end anastomosis is made (Fig. 19b).

Postoperative care. This parallels in every way that of the gastric cases. The only important difference is that the inlying duodenal tube is kept *in situ* for 4 to 5 days. No enemas are given. The patient is allowed mineral oil by mouth 2 days after the indwelling duodenal tube comes out.

MISCELLANEOUS RESECTIONS

There were 3 cases in this group: (1) a gastrojejunostomy for congenital cystic disease of the liver; (2) a jejunogastroplasty for carcinoma of the esophagus; (3) a duodenojejunostomy in a patient of 76 for obstruction in the retroperitoneal duodenum occasioned by a fixed irremovable carcinoma. All the patients recovered. In addition, there were 6 oblique end-to-end anastomoses in the jejunum, described as a part of the operative procedure in gastric resection for gastrojejunal ulcer.

Only one of the procedures listed above is sufficiently interesting to merit special mention, namely: jejunogastroplasty for esophageal carcinoma. The procedure is not difficult to perform and the jejunum serves as a satisfactory tube for feeding. What is of most importance, with reference to the problem of ultimate reconstruction of the esophagus, is that the oral end of the jejunum can be placed ordinarily well above the xiphoid process near the nipple line. Further, final union between a skin tube and the jejunum can be achieved more readily than with the stomach. An oblique end-to-side anastomosis is made between the aboral end of the jejunum and the stomach and intestinal continuity is established by an oblique end-to-end anastomosis. In all, 5 such jejunogastroplasties have been made (3 prior to and 1 since this series) without hospital mortality.

[1] Latterly, in right sided lesions, I have been making oblique end-to-end anastomoses between the ileum and the colon. It is the simplest procedure.

TABLE I.—DIVISION OF MATERIAL AND HOSPITAL MORTALITY

		Number of cases	Hospital deaths	Cases of recovery	Per cent mortality
I. Gastric resections		83	3	80	3.6
A. Ulcer	48		0	48	0
B. Neoplasm	35		3	32	8.5
1. Carcinoma	30*				
2. Lymphosarcoma	1				
3. Leiomyoma	1				
4. Polyps	3				
II. Colon resections		14	1	13	7.1
III. Miscellaneous resections		3	0	3	0
Totals		100	4	96	4.0†

*During this period of time there were 4 additional primary carcinomas of the stomach explored (see text), in which resection was not done. The resection rate for the gastric malignancies, therefore, is 88.5 per cent (31 out of 35 cases). Jejunostomy for feeding was done in the 4 cases explored, but not resected. There was no hospital mortality.

†Two frail old ladies, among the very last to be operated upon in this series of 100 closed resections, have since died, and the mortality for the series is, therefore, 6 per cent and not 4 per cent, as stated in the table. One of these, Mrs. A. S., Univ. Hosp. No. 674416, a very feeble patient of 74 operated on for carcinoma of the stomach, died on the 44th day of hospitalization from passive congestion and heart failure. The other patient, Mrs. L. T., Univ. Hosp. No. 665645, aged 71, was operated upon for a para-esophageal lesion, believed to be carcinoma, but which proved to be a benign ulcer. Her immediate convalescence was satisfactory. Death occurred 29 days after operation from mesenteric arterial and venous thrombosis of a loop of terminal ileum. This latter case is the only mortality in the benign ulcer group. Since the time of this report an additional 23 primary gastric resections have been done for ulcer without mortality, including 4 bleeding duodenal ulcers, 4 gastrojejunal ulcers, and 1 gastrojejuno colic fistula.

MORTALITY

The immediate results of operation on the 100 consecutive patients with closed anastomosis are shown in the accompanying tables. There were 4 deaths.[2] Among the gastric resection group (83 cases) there were 3 deaths (3.6 per cent). In 48 benign ulcers, including duodenal, gastric, para-esophageal (4), and gastrojejunal (5), there were no deaths. There was 1 death among 14 colon resections and none in a group of 3 patients with miscellaneous types of anastomoses.

OBSERVATIONS

It is to be observed that 3 of the 4 deaths were due to surgical blunders. The 2 avoidable deaths in the gastric malignancy group were due to technical errors, the 1 to obstruc-

See footnote accompanying Table I.

TABLE II.—ANALYSIS OF CAUSE OF DEATH IN FATAL CASES

Date of operation	Name, age and sex	Univ. Hosp. No.	Diagnosis	Survival period	Cause of death	
					Unavoidable	Avoidable
5-31-40	S. S. 59 yrs. M.	U. H. 695813	Carcinoma stomach (favorable)	48 hours		Distention of proximal loop of gastro-jejunal anastomosis
8-27-40	F. C. 52 yrs. M.	U. H. 654633	Pyloric carcinoma and gastrojejunal ulcer (favorable)	6 days	Coronary thrombosis	
8-29-40	F. R. 72 yrs. M.	U. H. 698763	Carcinoma stomach (unfavorable)	13 days		Duodenal fistula and peritonitis
9-25-40	C. K. 62 yrs. M.	U. H. 699541	Perforated carcinoma of colon (unfavorable). Colon resection and excision of right kidney and ureter	6 days		Peritonitis-anastomosis intact

tion to the afferent duodenojejunal loop in the gastrojejunal anastomosis, the other to an insecure closure of the duodenum. The problem of closing the open duodenum in the socalled irremovable duodenal ulcer, or in the duodenal ulcer with massive hemorrhage, constitutes the most difficult task that the surgeon is called upon to deal with in gastric resection. There were 9 instances of perforation of the posterior duodenal wall in the ulcer resection group, necessitating the type of closure illustrated in Figure 5. There were 2 additional cases in which sealed perforations were present in the anterior duodenal wall demanding sacrifice of a more liberal portion than usual of the anterior duodenal wall. Yet, there were no deaths among these patients. Whereas, the mortality in the gastric neoplasm group was 8.5 per cent, the mortality should have been, when the avoidable deaths are deducted, 2.8 per cent.

The death in the colon resection group occurred in a patient with an adherent lesion perforated onto the right ureter and the retroperitoneal duodenum. Autopsy showed the suture lines to be intact. Peritonitis occurred from the apparently minimal contamination (no visible spillage) attending dissection and manipulation of the perforated lesion. Had the initial dissection envisaged the plan of excising the kidney, instead of accepting finally its necessity, the area of perforation would have been excised rather than broken into.

This is a problem peculiar to colon resections apparently. In the gastric resection group for malignancy, several instances were dealt with in the manner illustrated in Figures 4, 5, and 12, with evident source for contamination, but without apparent increase of risk to the patient.

LOCAL USE OF SULFANILAMIDE

Implantation of sulfanilamide (4 grams) was made about the site of contamination in the colon case referred to above, but without obvious protective value. My associate, Dr. Richard L. Varco, following the lead of Jensen, Johnsrud, and Nelson (1939), has implanted sulfanilamide about complicated gastro-intestinal anastomoses in dogs with considerable lessening of the mortality of such operations. This suggestion has been carried over into the colon resection group and into those instances among the gastric resection group for malignancy in which frank breaks in the aseptic technique were demanded by the type of case illustrated in Figure 12.

Varco appears to have established for the dog, at least, that the local implantation of sulfanilamide about the anastomosis has real value. It is to be recalled, however, that dogs tolerate large doses of sulfanilamide without evincing evidence of liver damage. Further, dogs do not acetylate or inactivate a portion of the sulfanilamide administered as does man. Varco's studies suggest, as did Jensen's earlier work, that local implantation is superior to its para-oral administration.

This aspect of the problem in man deserves thorough study. A local bacteriostatic or bactericidal agent which would be absorbed slowly, exerting a prolonged local effect, which could be left in the peritoneal cavity at the time of operation would be a great boon to the surgeon in dealing with the sealed perforation

in colon resections. My experience suggests that the surgeon may excise sealed perforated gastric malignancies without apparent increase in the surgical risk. In the colon group, he must bend every effort *to excise unopened* the site of perforation. Should the surgeon open into a perforated lesion, placement of sulfanilamide (4 grams) on a gauze sponge, wrapped carefully about the area, should be done at once. In the fatal colon resection in the group, sulfanilamide was placed at the site of perforation and about the anastomosis on completion of the operation—about 2 hours after the break in the aseptic technique occurred.

In the colon resection group, including the patient who died, perforation of the colonic malignancy into an adjacent loop of small intestine was observed 3 times. Carcinoma of the transverse colon, adherent to the stomach (2 cases), may necessitate simultaneous excision of a portion of the gastric wall. In large gastric malignancies, however, invading the transverse colon (1 case in this series) gastric resection and excision of the involved portion of the transverse colon, with performance of colostomy were carried out at the first operation, with secondary establishment of continuity in the large bowel.

REMOTE RESULTS

This communication is essentially technical in character and does not propose to deal with the remote results of operation. A few general comments bearing upon the choice of operative procedure, however, may not be out of place.

THE PALLIATIVE OPERATION

Excision of the primary lesion with liver metastases was done twice in the gastric malignancies in this series and once among the colon group. A number of other obviously palliative procedures were done in the gastric group in which resection was performed in the presence of metastatic lymph nodes which could not be removed, when nodules were present over the diaphragm or in the cul-de-sac. One case is of particular interest in this connection. A synopsis of the patient's history follows.

Mrs. C. H., University Hospital No. 699368, aged 38 years, was admitted to the gynecologic service for a large abdominopelvic tumor the size of a 6 months' pregnancy. The tumor (Fig. 22a) was excised by Dr. J. L. McKelvey, professor of obstetrics and gynecology, and Professor Robert Meyer, pathological attaché to Dr. McKelvey's department, stated that despite the absence of gastric symptoms the adenocarcinoma transplanted onto the excised ovaries and uterus was a socalled Krukenberg tumor and had its origin undoubtedly in the stomach.

After recovery from the initial operation, x-ray examination of the stomach was carried out—a small lesion being found on the lesser curvature. Gastroscopic examination confirmed this observation, and 3 weeks after the first operation gastric resection was performed. A small lesion difficult to palpate but with a few juxtapositional lymph nodes was found (Fig. 22b). Because of the obvious lack of serosal involvement, it was postulated that the lesion probably had spread widely in the submucosa and mucosa (Verbrugghen), and that excision of the entire lesser curvature was necessary. The only distant metastasis made out was a small nodule in the right lobe of the liver. When it was uncovered by retraction of the right costal margin on completion of the operation for the implantation of a radium seed, it was observed to be a hemangioma. The pelvis was entirely free from tumor.

Is palliative surgery of this variety justified? I do not know and do not defend the thesis, though I am trying to probe its rationale. It is obvious that greater risks are accepted for such patients than in the ordinary case. I believe such obvious transgressions of the usual orthodox indications for operation can be justified only if the risks of the procedure are not far out of line with the hazards accepted by standard risks. It is obvious that in the ultimate analysis the surgeon cannot in such a group demonstrate the same accomplishment as in the select cases.

I must confess to a feeling of some disappointment in knowing that 2 of the palliative gastric resections are exhibiting already, within 4 to 6 months of the time of resection, definite evidence of progression of their disease. Yet, I am cheered on to continue these apparently aggressive operations by the occasional patient who survives a palliative resection done in the presence of remaining metastatic lymph nodes for years. I have observed survival for a year, following excision of a portion of the retroperitoneal duodenum for a polypoid bleeding tumor when

metastases were present in the liver at the time of operation. Another patient survived primary excision of the colon 15 months under the same circumstances. One patient with obstruction of the small intestine from a carcinoma still survives 2 years and 6 months after a short circuiting operation. The local lesion was not excised because of large metastases in the liver. The patient continues to hold his 70 pound weight gain since operation. What mechanism has restrained the growth of the neoplasm? If we only knew and could imitate or augment the mechanism, the cancer problem would be nearer solution.

The remote results in malignancies, favorable for excision, in the stomach or colon need no defense. Our own experience (Bergh) corroborates the published opinion of a number of writers on this score.

DIFFICULTY OF DISTINGUISHING GASTRIC ULCER AND CARCINOMA

Earlier recognition is still an obviously important item to anyone who reviews critically his own material. In this connection, it probably should be said that too large a number of gastric cancers come to operation after they have been treated for too long periods of time as gastric ulcer. The inability to distinguish between ulcer and carcinoma in certain cases is only too well known. It would appear that surgical excision holds out less risk to such patients than the "wait and see" policy. In this series there were several cases in which the histologic diagnosis had to be awaited before the true nature of the lesion was known. In such doubtful cases, more often than not, the lesion turns out to be an ulcer, but there are in this small series, 6 cases that proved to be malignant when the preponderant preoperative evidence favored a benign lesion.

The small juxta-esophageal lesion is a particular problem (Finsterer, Rieder, Walters). Of the 5 in this series 4 proved to be benign. A benign ulcer here in our experience may be accompanied by a low free gastric acidity. A malignant prepyloric ulcer, however, may exhibit high gastric acidity. Achlorhydria to histamine stimulation is still a very important adjunct to the clinical, x-ray, and gastroscopic diagnosis of gastric malignancy.

RESULTS OF RESECTION FOR ULCER

An opportunity to follow patients in the outpatient clinic who have undergone operation for ulcer is a very gratifying and reassuring experience. The question of what might be expected of gastric resection is beyond the limits of this discussion and has been dealt with, in part, elsewhere (27). The majority of the ulcers in the series reported here had resection of 75 to 80 per cent of the stomach, including pylorus and antrum, after the Billroth II plan of operation.

SUMMARY AND CONCLUSIONS

The closed or aseptic method of anastomosis is an eminently satisfactory procedure for accomplishing continuity after resection in any portion of the alimentary canal. The surgeon is still the most important factor in the operative mortality of resections. In the 4 deaths which occurred in this series of 100 patients, there was only 1 unavoidable death (coronary thrombosis). The planned operation with studied thought lent to every detail of the procedure pre-operatively is the most important factor in achieving a reasonable mortality. Good anesthesia, trained and alert associates, intent on avoiding the numerous pitfalls which may overtake the patient in the convalescent period, and a seasoned experience, all play significant rôles in keeping operative hazard at a minimum. The blunders of the surgeon during operation, whether of commission or omission are usually beyond recall and are irreparable. On the contrary, mistakes made in postoperative management are amenable often to adjustment or correction by timely recognition, permitting salvage of the situation.

There were 3 deaths in the entire gastric resection group (83 cases), a mortality of 3.6 per cent. In the ulcer group (48 cases), including duodenal, gastric, juxta-esophageal, and gastrojejunal, there were no deaths. For the gastric neoplasm group (35 cases), the mortality (3 cases) was 8.5 per cent. One death in 14 resections occurred in the colon cases (7.1 per cent). In the miscellaneous resections (3 cases) there were no deaths. The resection rate for gastric malignancy in this group was 88.5 per cent (31 out of 35 cases).

Resections for ulcer, it is believed, should be achieved with a mortality of about 2 per cent (unavoidable mortality). In the malignant group (both stomach and colon) avoidable deaths, due to errors of the surgeon, can never be eliminated entirely, probably. Yet it should be possible to perform both gastric and colonic resections with a mortality of approximately 5 per cent (unavoidable deaths).

Obstruction of the afferent loop in gastrojejunal anastomosis, without gangrene, hitherto undescribed, is pointed out as a likely important factor in the cause of mortality after gastric resection. Death, through this agency, may occur also after simple gastrojejunostomy in the presence of high grade pyloric obstruction. Death occurs about 48 hours after operation from hyperthermia. The condition may be reproduced experimentally in the dog. Placement of a forked-type of catheter, to which suction is applied, in the ascending and descending limbs of the anastomosis eliminates the hazard of distention to the proximal loop.

The principles of pre-operative and post-operative management in patients undergoing gastric or colonic resections are reviewed. In particular, it is suggested that the bedside weighing scale be employed as a guide in ascertaining the status of hydration in poor risk patients. The loss of fluid by vaporization is so variable a factor that the urine output cannot be used safely as the gauge for the quantity of fluid to be given. The compensation of poor risk patients given fluid by the usual standards of administration may break. Only the weighing scale can tell in patients with low urine output whether the water has been vaporized or is collecting in the extracellular fluid spaces. The latter occurrence may threaten disaster in patients with poor cardiac reserve.

The aseptic anastomosis, it is believed, extends the range of operability in resections in the alimentary canal without increasing the hazards materially over those accepted by standard or select risks.

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THE SURGICAL TREATMENT OF GASTROJEJUNOCOLIC FISTULA

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THE most dreaded complication of gastro-enterostomy is the formation of a common fistulous communication between the stomach, jejunum, and colon due to the perforation of a stomal or jejunal ulcer into the adherent colon. Very seldom the lesion may result spontaneously from carcinoma of the stomach or colon which traps the adjacent hollow viscera and ulcerates through their walls. In any event the consequences of such a union are disastrous. Pain may be present but, curiously enough, may disappear on formation of the fistula. Severe gastric indigestion occurs with belching of foul smelling gases and, at times, vomiting of material resembling colonic contents. Diarrhea is the rule and may be severe. Undigested particles of food may be noticed in the stool. Loss of weight begins at once and is often rapid and extreme. Anemia, avitaminosis, and serious fall in serum proteins develop and in severe diarrhea there may be dehydration and marked imbalance of chemical plasma structure. In a matter of months or even weeks, the patient's physical condition is reduced to a point which renders extremely dangerous any attempt to carry out the procedures necessary for ablation of the fistula and restoration of continuity. Furthermore all tissues adjacent to the fistula are often edematous, inflamed, and heavily infected, in this manner increasing the operative difficulties and inviting postoperative complications.

That this picture is not overdrawn is shown by the mortality figures. No series, personal or collective, thus far reported has shown a mortality of less than 25 per cent and from this it has ranged up to 63 per cent in most skillful and experienced hands. I suspect that a complete collective study, if it could be made, would reveal the situation as even worse since I have found that single sporadic cases in which operation was done in various clinics by methods hitherto employed have almost invariably resulted fatally and are not reported.

The chief causes of death are shock, peritonitis, pulmonary complications, leakage, usually from the repaired colon, embolism, and hemorrhage. Almost all patients coming to operation have already reached the stage of severe malnutrition, either because of failure to realize the rapid deterioration which follows formation of the fistula or because of prolonged ineffectual efforts to control it by medical management. There is no medical treatment for this condition other than the measures necessary for rehabilitation prior to surgical attempt at cure. On the other hand, to operate precipitately without rehabilitation is almost equivalent to a death warrant.

The measures available are principally, transfusions of whole blood and especially plasma, a high vitamin, high protein and caloric diet, and bed rest. Opium is of value in reducing intestinal irritability and, for diarrhea such agents as kaolin and bismuth are helpful. Alkalies are not always of value and may be harmful as tending to increase the danger of hypochloremia. By such means, carefully carried out, Coller (personal communication) reduced his mortality from about 40 per cent to approximately 12 per cent in simple reconstruction operations.

But not all patients can be rehabilitated so long as the fistula is actively conveying colonic contents into the stomach and jejunum. A plan is now presented by which this can be prevented, whereby in the vast majority of cases symptoms can be completely alleviated and rapid restoration of the patient effected to a state in which any radical procedure indicated to remove the fistula and also deal with the ulcer diathesis can be done with no higher

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mortality than is inherent in the procedure itself.

This plan requires the adoption of preliminary colostomy proximal to the fistula as a first stage. In May, 1938, I presented before the American Surgical Association observations on the value of preliminary colostomy in the correction of gastrojejunocolic fistula. This paper cited 3 cases of ultra-severe fistula, 2 of my own and 1 of Colp, who adopted the suggestion originally made in an earlier report of the first case. For the argument, reference should be made to the paper in the *Annals of Surgery*, October, 1939, but the experience gained pointed unmistakably to the conclusions drawn. In order to check those conclusions for the purposes of this communication, a letter was sent to each member of the American Surgical Association to ascertain how often the plan advocated had been employed, with a note of results and observations. The response was prompt and practically complete. No attempt was made to gather the entire experience of the membership with this lesion as it was believed that an adequate cross-section of results with other plans existed in the literature. The replies have brought the total of patients treated by preliminary colostomy followed by resection or restoration to 15. All were males who had had a previous gastro-enterostomy for ulcer with the single exception of Morton's case of spontaneous formation of this lesion due to a malignant tumor of the stomach. This patient was a female. Ten were treated in the second stage by gastric resection, 5 by simple restoration. Fourteen recovered, 1 died, a mortality of 6.6 per cent. A brief summary of the cases listed under the name of the contributor is as follows.

CASE REPORTS

CASE 1. (D. B. Pfeiffer.) Male, aged 34 years, had had gastro-enterostomy for duodenal ulcer 4 years previously. The patient had improved until the onset of the present symptoms 5 months before admission. He complained of severe diarrhea, foul belching, and a voracious appetite. His weight loss had been 30 pounds. There was moderate anemia. The abdomen was boggy, slightly distended, and peristalsis hyperactive. At x-ray examination barium passed through the pylorus but mostly through the anastomosis and with incredible rapidity through the small intestine. No barium could be seen passing directly from the stomach into the colon but by barium enema it was seen to enter the stomach at a point proximal to the splenic flexure. October 2, 1936, an exploratory operation was performed. The stomach, jejunum, and colon were found matted together; there was considerable free fluid. All the adjacent tissues were acutely inflamed and edematous. There were two separate jejunal ulcers distal to the anastomosis. Radical surgery was absolutely contra-indicated. An ascending loop colostomy was done and was opened on the third day. *All the symptoms disappeared at once.* After the contents of the distal colon had been expelled, there were no further bowel movements. The patient gained 50 pounds in 4 months. On February 1, 1937, operation was performed. Inflammatory changes were absent; there was no ree fluid; the separate jejunal ulcers had healed. The original ulcer had apparently healed. The anastomosis was taken down without difficulty and repair of the stomach, jejunum, and colon carried out. There was marked distention following the operation. Because of the fear of leakage from pressure, a simple pursestring jejunostomy was done on the third day. Further convalescence was uneventful. The patient has remained well to the present time.

CASE 2. (D. B. Pfeiffer.) Male, aged 39 years, had had an appendectomy in May, 1927. Simple suture for perforated duodenal ulcer had been performed in August, 1929. A recurrent duodenal perforation developed in February, 1937. Suture of the perforation and a posterior gastro-enterostomy were done. Following episodes of pain in the left lumbar region the patient had developed symptoms of a gastrojejunocolic fistula 1 month before admission to the hospital, June 3, 1938. His present symptoms included diarrhea, fecal vomiting, and belching of foul gas, diffuse abdominal pain, and a more than 10 pound weight loss in a month. There were present moderate anemia, epigastric tenderness, and hyperperistalsis. Roentgenographic examination showed the opaque medium leaving the stomach through both pylorus and anastomosis and from jejunum directly into colon. A barium enema showed prompt entrance of material from the transverse colon into the stomach and jejunum. On June 8, 1938, an exploratory operation was performed. The entire area of the anastomosis and transverse mesentery was found to be inflamed and edematous. A loop colostomy of the mobilized ascending colon through a muscle splitting incision in the flank was done and opened 5 days later. *All digestive symptoms disappeared.* Normal stools were obtained by colostomy, occasionally by rectum. The patient had a marked gain in weight and remained well. He was readmitted 4 months later for the second operation. The pylorus was patulous and the old ulcer apparently had healed. Inflammatory changes at the site of the fistula were entirely absent. Disconnection of the anastomosis and a fistula measuring 1 by 3 centimeters were disclosed. The defects were closed.

A pursestring jejunostomy was done; recovery was uneventful. The spur was destroyed, the colostomy closed, and the patient discharged 5 weeks after his admission. His original duodenal ulcer has been reactivated and resection has been advised. Our present opinion is that it would have been better judgment to have resected at the second operation.

CASE 3. (Dr. Ralph Colp.) Male, aged 49 years, had undergone a posterior gastro-enterostomy for duodenal ulcer on January 7, 1935. Recovery was uneventful. There were no symptoms for 3 years. Three months before his second admission, April 13, 1938, the patient began to have diarrhea, belching of foul smelling gas, and a rapid loss of weight. A barium enema revealed a gastrojejunocolic fistula. An ascending loop colostomy was performed on January 9, 1938, and was opened on the sixth day. *All symptoms disappeared.* The patient gained 18 pounds in 3 months. A fistula could not be demonstrated by x-ray examination. Operation was performed on July 16, 1938. A hard inflammatory mass involving stomach, jejunum, and colon was disclosed. There was a healed jejunal ulcer 12 inches below stoma. *The fistula had closed.* A subtotal gastric resection was done by the Hofmeister antecolic method. Repair of the colon and end-to-end union of the jejunum was carried out. There was a moderate postoperative reaction, but the patient was well by March, 1939, and had gained 25 pounds.

CASE 4. (Dr. J. H. Gibbon, Jr.) Male, aged 38 years, had undergone a posterior gastro-enterostomy for ulcer in 1924. The patient entered the Pennsylvania Hospital in March, 1939, with a marked diarrhea of 6 weeks' duration. His weight was 116 pounds; there had been a loss of 10 pounds in 6 weeks. Tuberculosis of the right upper lobe was present; the sputum was positive. A barium enema showed rapid filling of the stomach from the colon. Reverse passage was not seen. Medical management for 8 weeks resulted in no diminution of diarrhea and a further weight loss of 10 pounds. On May 29, an ascending colostomy was done. Convalescence was complicated by the appearance of a tender inflammatory mass in the left lower quadrant with fever which gradually subsided. The diarrhea continued but his weight remained stationary at 97 pounds. As a result of intensive intravenous therapy with blood and plasma transfusions, his weight picked up 10 pounds in 2 weeks, although he continued to have one or two movements by rectum and lost considerable food by direct passage from the stomach through the fistula into the colon and by reverse peristalsis from the distal end of the colostomy. On August 11, 1939, a gastric resection with removal of the fistulous area in one mass was carried out with resection and anastomosis of both the jejunum and colon. Operative recovery was satisfactory. Two months later a small intestinal obstruction from an adhesion in the pelvis was relieved by operation. At present, 1 year later, the colostomy is closed and his general condition is excellent.

CASE 5. (Dr. S. C. Harvey.) Male, aged 40 years, had had a posterior gastro-enterostomy in 1924. Moderate relief was obtained for 2 years, then massive hemorrhage developed. In October, 1926, a pylorectomy was done, restoration by Roux en Y. Relief was obtained only for 1 month. Reoperation was done in 1929. The patient stated that no ulcer was found. Cholecystectomy for pericholecystic adhesions was done. Improvement was short, followed by ulcer symptoms and repeated tarry stools. He was admitted to New Haven Hospital in December, 1929. Considerable relief was obtained by medical management, but his symptoms recurred and an operation was done elsewhere for jejunal ulcer. Excision of the ulcer was carried out with resection of the old gastro-enterostomy and the making of a new one. His symptoms persisted, and the patient was readmitted to New Haven Hospital in June, 1937. Again the patient improved on the Sippy regimen. He was readmitted 2 years later; 10 weeks previously he had begun to have severe diarrhea, passage of undigested food in the stool, a rapid loss of 22 pounds in weight. A gastro-intestinal series revealed a gastrojejunocolic fistula. His general condition still remained reasonably good. On June 16, 1939, a preliminary double-barreled ileostomy was done. On June 30, 1939, the Hofmeister type of gastric resection was carried out. Recovery was uneventful. An end-to-end anastomosis of the colon was done. The ileostomy was closed on September 6, 1939. On November 7, 1939, the patient was symptom free.

CASE 6. (Dr. J. T. Priestley, Mayo Clinic.) Male, aged 48 years, had had a posterior gastro-enterostomy for ulcer in 1933. Temporary relief had been obtained. For the last 3 years, the patient had had severe diarrhea with passage of undigested food and a loss in weight of 30 pounds. His serum protein was 3.7. On August 3, 1939, a proximal transverse colostomy was done. Ascites was present, all the tissues were edematous. General improvement resulted but leakage of gastric contents from the distal limb of the colostomy occurred until this was plugged. A transfusion was given on August 24, 1939. Serum protein was 5.9. A partial gastrectomy by the posterior Pólya method and closure of the colon and jejunum were carried out. Convalescence was uneventful. On December, 1939, the patient was well and had gained 35 pounds.

CASE 7. (Dr. C. Mathewson, Jr.) Male, aged 50 years, had undergone posterior gastro-enterostomy for ulcer in May, 1920. The patient was well for 2 years, then recurrence of the ulcer symptoms took place. Two months before his admission to San Francisco Hospital, severe diarrhea began with vomiting of foul material and rapid loss of 50 pounds in weight. A barium enema showed a gastrojejunocolic fistula. Operation was performed on June 11, 1936. The colon was detached and repaired, the jejunum repaired. The gastro-enterostomy was not taken down. Convalescence was stormy. The diarrhea stopped but ulcer symptoms persisted. On his re-

admission to the hospital, September, 1939, a gastrojejunocolic fistula again was present. There was further loss of weight (present weight 97 pounds, best weight 180 pounds). Hyperperistalsis was present. An operation was performed on October 10, 1939; an exteriorized cecostomy was done. *All the symptoms disappeared.* The patient gained 34 pounds in less than 2 months. A second operation was carried out on January 16, 1940. Inflammatory changes were absent. The colon was freed and closed. A fistula 3 centimeters in diameter was disclosed. A gastric resection by the posterior Pólya method was performed. Recovery was uneventful. The patient has been well to date.

CASE 8. (Dr. C. Mathewson, Jr.) Male, aged 39 years, had had a perforated duodenal ulcer in 1929. Closure of the ulcer and a posterior gastroenterostomy were carried out, but the ulcer symptoms persisted. In 1938 a marginal ulcer was diagnosed. The patient was readmitted January 31, 1940, with symptoms of a gastrojejunocolic fistula of 2 months' duration. Severe diarrhea was present; pain had disappeared but there was much belching of foul gas and some vomiting. A considerable loss of weight had occurred. Hyperperistalsis was present. A barium enema showed a gastrojejunocolic fistula; barium by mouth did not show it. Barium passed from the stomach to the colon in 30 minutes. On February 3, 1940, a loop transverse colostomy was made. *There was only one stool by rectum after the colostomy was opened.* There was a gain of 16½ pounds in weight in 5 weeks. Re-operation was done on March 3, 1940. Inflammatory changes were absent. The colon was detached and repaired. A fistulous opening 5 centimeters in diameter was found. A posterior Pólya resection was performed. Some wound infection developed. Otherwise recovery was uneventful. A barium enema later showed that the repaired colon had opened to some extent (had colon been functioning this would in all probability have caused death). Seven weeks later, however, the colon was closed with good recovery.

CASE 9. (Dr. R. R. Graham.) Male, aged 42 years, had had a posterior gastro-enterostomy 3½ years previously for severe ulcer symptoms and repeated hemorrhages. Improvement took place for 6 months, then recurrence of the symptoms developed. Three weeks previously the patient had felt something give way in the abdomen followed by vomiting which became foul. Diarrhea which scalded the skin around the anus occurred. The pain ceased but the patient lost 20 pounds in 3 weeks. On September 9, 1939, an ascending loop colostomy was done. *All of the symptoms stopped.* The patient gained 18 pounds in 1 month. ("This man's progress following the colostomy was unbelievably delightful. After a week, one could wash the distal colon without any going into the stomach." R.R.G.) On October 25, 1939, re-operation was performed. A slight edema was still present about the area of the lesion but not of any moment. The colon was separated, a fistula 1 by 1½ inches was found. The colon was repaired, and the jejunum transected and anastomosed. A subtotal gastric resection by anterior Pólya method was performed. Convalescence was complicated by massive collapse of the left lung with some pneumonia but recovery was good. Fistula closure, 3 weeks later, was not entirely successful due to infection but was completed readily later. Recovery to date has been complete.

CASE 10. (Dr. A. W. Allen.) Male, aged 56 years, had had a gastro-enterostomy 10 years previously. Diarrhea and typical symptoms of gastrojejunocolic fistula were present. The patient had lost 30 pounds. On September 14, 1939 a right colostomy was performed. The patient's general condition was much improved though the 3 pound weight gain was not impressive. On January 6, 1940, a subtotal gastrectomy was performed with transection and anastomosis of both the jejunum and colon. Prompt and uneventful recovery occurred. A gain of 27 pounds in 6 weeks took place. Colon has closed and patient is in excellent health.

CASE 11. (Dr. H. Trout.) Male, aged 40 years, had been treated at Veterans Hospital, and the records are sketchy. Posterior gastro-enterostomy had been performed 4 to 5 years previously for ulcer. Symptoms of marginal ulcer had been present for about 18 months; foul breath, diarrhea, vomiting of fecal material for the past few months. Medical management gave no improvement. A gastrojejunocolic fistula was demonstrated. An exploration was done in August, 1939. The general condition of patient was wretched. He was little else than skin and bones. Local edema and inflammation were present around the lesion. An ascending loop colostomy was performed. ("I don't think I ever saw a patient's general condition improve more quickly." H.T.) A second operation was done 5 to 6 months later. The patient's general and local condition were entirely satisfactory. Excision of the fistulous tract and restoration of continuity were effected. Recovery was uneventful. The patient was placed on ulcer regimen to prevent reactivation of the original ulcer but he has remained well and has gained 30 to 40 pounds in weight.

CASE 12. (Dr. J. J. Westermann.) Male, aged 42 years, had had a Roux type of gastro-enterostomy (no ulcer established) in 1934. In 1936, an exploration was carried out for a supposed marginal ulcer. The attempt was abandoned "because of adhesions." In 1938 (J.J.W.) the gastro-enterostomy was undone, the ulcer was excised, an entero-anastomosis and high gastro-enterostomy were performed thus closing the previous stoma. In 1939, a jejunal ulcer developed 1 in. below the stoma. The gastro-enterostomy was undone, the jejunum was repaired pylorectomy and posterior Pólya carried out. A subtotal resection was decided against because of the technical difficulties. The patient's symptoms reappeared and a gastrojejunocolic fistula occurred in January or February, 1940. In May, 1940, a transverse colostomy was performed. The pain

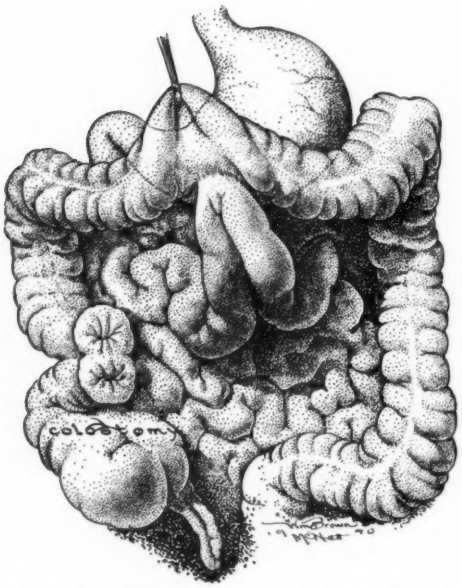

Fig. 1. Two stage operation for gastrojejunocolic fistula. Pfeiffer (semidiagrammatic) exploration of lesions, ascending loop colostomy.

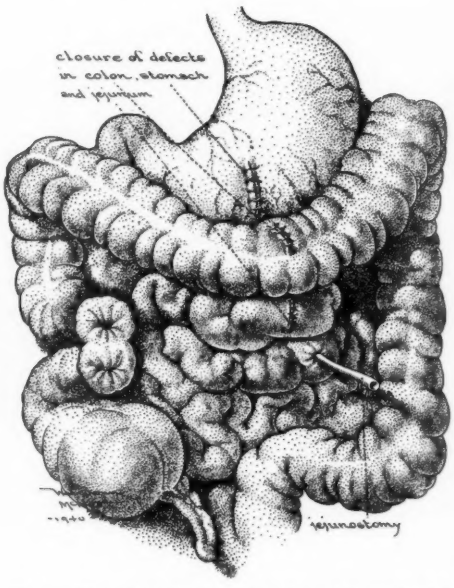

Fig. 2. Two stage simple restoration with repair of defects in stomach, colon, and jejunum. Jejunostomy optional.

was relieved, appetite and nourishment improved, although there was loss of liquids through the colostomy. On July 9, 1940, re-operation was carried out. A subtotal gastric resection, a Pólya antecolic repair of the jejunum, resection of the colon and anastomosis, jejunostomy were done. ("Convalescence very smooth. I attribute the survival of this patient to the presence of the colostomy." J.J.W.)

CASE 13. (Dr. J. J. Morton.) Female, aged 53 years, complained of increasing epigastric pain, nausea, and vomiting for 6 months, eructations but no diarrhea, and a weight loss of 25 pounds. A barium enema showed rapid passage from splenic flexure of the colon to the stomach and jejunum. Barium meal showed a fistula from the post. wall of the stomach to the jejunum and colon. On May 15, 1940, an exploration was carried out. A large mass, the size of a large orange and thought to be carcinomatous, was revealed which involved the stomach and bowel but was otherwise free. A transverse colostomy following the Devine method was done. The patient's convalescence was reasonably uneventful. Fifteen days later the jejunum was freed and repaired. The gastrocolic mass was excised. A subtotal gastrectomy was performed by the Hofmeister operation; end-to-end union of the colon was carried out. ("Surprisingly comfortable convalescence." J.J.M.)

CASE 14. (Dr. J. D. Bisgard.) Male, aged 42 years, was admitted to the hospital in July, 1940. A gastro-enterostomy had been done 8 years previously for duodenal ulcer. He had remained well for 7 years. His history indicated the development of a jejunal ulcer 1 year previously and a gastrojejunocolic fistula 3 weeks previously. In that period he had had severe diarrhea and had lost 38 pounds. Fluid and chemical balance was secured and an exteriorizing cecostomy was performed. Prompt cessation of the diarrhea and a gain of 12 pounds in 3 weeks resulted. On August 7, 1940, the gastro-enterostomy was taken down, end-to-end aseptic anastomosis of the jejunum and of the colon was performed. The patient's convalescence was uneventful.

CASE 15. (Dr. F. W. Bancroft.) Male, had a gastrojejunocolic fistula of some duration. General condition of patient was unsatisfactory. In May, 1940, an ascending colostomy by the Devine method was carried out. There was a constant irritating discharge from the distal opening. The patient continued to lose weight and strength. In July, 1940, because improvement seemed otherwise impossible, he was re-operated upon. A very large fistula was found and a difficult penetrating ulcer into pancreas. Subtotal resection was carried out. The patient died the ninth day after operation because of a leaking duodenal stump with a subphrenic abscess. ("I would have done much better if I had done a Devine type of pyloric exclusion instead of attempting to dissect the duodenum." F.W.B.)

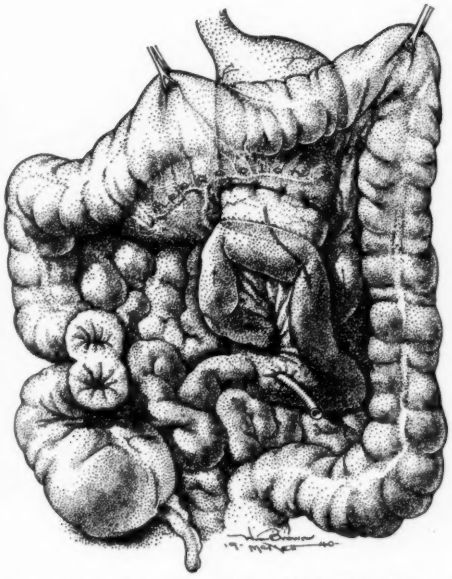

Fig. 3. Second stage, second method (preferred), partial gastrectomy, excision of fistula, repair of jejunum, restoration of continuity (Pólya).

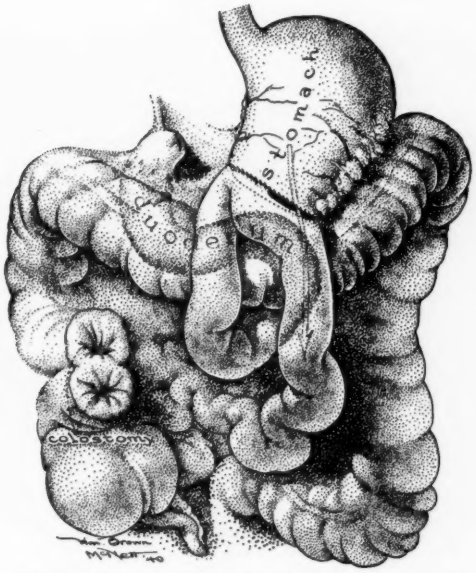

Fig. 4. Preferred method. Subtotal gastrectomy; antecolic gastrojejunostomy (Pólya or Hofmeister).

EVALUATION

It is now possible to re-examine the conclusions and recommendations originally made in the light of the findings in the present series of 15 cases. These additional cases represent the experience of a relatively small group of American surgeons with this plan in a period of only a little more than a year.

The important conclusions referred to were that: (1) the loss of food from the stomach into the colon is ordinarily not significant; (2) the rapid weight loss and general deterioration of physical condition is not due to starvation from this food loss nor is the diarrhea caused by the entrance of gastric contents into the colon; (3) the important cause of serious symptoms is the continued entrance of colon contents into the upper gastro-intestinal tract; (4) loop colostomy proximal to the fistula abolishes symptoms, thus permitting rehabilitation to the point that adequate corrective surgery may safely be done upon the fistula.

When these statements are considered in order, it is found that no detailed information as to food loss into the colon is available in 3 cases except that symptoms are said to have subsided after colostomy. In 3, however, it is stated that no bowel movements occurred after the colostomy, in 1 instance for as long as 4 months. Yet each of these patients had been having severe diarrhea with marked loss of weight. There was prompt gain of weight in each case. In 5 patients there was more or less loss into the colon but diarrhea ceased and weight gain was about as satisfactory as in those patients who showed no loss at all into the colon. The explanation of this curious observation is to be found in the fact that the entrance of colonic contents into the upper gastro-intestinal tract sets up irritation and violent hyperperistalsis. This is a common clinical observation and is confirmed by the roentgenologist. In my first case Stewart observed barium to pass in a rush from the upper jejunum to the lower ileum in 3 minutes. Mathewson has given me the notes of a case of fistula in a patient suffering also from active pulmonary tuberculosis upon whom he has performed the preliminary colostomy with

marked improvement in general condition and cessation of diarrhea. The second stage is being deferred for maximum improvement. The remarkable confirmatory observation in this case came about through the difficulty in maintaining the colostomy as a complete one. On two occasions the colostomy retracted and both times the re-entrance of colon contents into the distal loop caused diarrhea. On both occasions repair of the colostomy was followed by stoppage of diarrhea. Mathewson states (personal communication) that experimental work inspired by this observation confirms that the entrance of colonic contents into the jejunum causes diarrhea. This then may be the full explanation of the diarrhea and appearance of undigested material in the stools so often noted. In addition to the disturbance of nutrition due to hyperperistalsis, disturbed digestion, and absorption, it is highly probable that the absorption of the toxic products present in the colon when introduced into the upper digestive tract must have a deleterious effect upon the general condition.

But it is necessary to state that in some cases there may be considerable loss directly into the colon. Priestley and Westermann each noted annoying loss of fluids from the proximal end of the colostomy, but in the first instance it was stopped by plugging and in the second was not serious. In Gibbon's patient there was large and serious loss into the colon after colostomy with continuance of diarrhea and lack of the prompt and striking improvement almost uniformly noted. However, this patient had active pulmonary tuberculosis. After the colostomy some sort of intra-abdominal inflammatory complication occurred with formation of a mass in the left lower abdomen which gradually subsided. In spite of this, improvement was slowly brought about aided by intravenous vitamin treatment and he was able successfully to make a gastric resection. Note, however, that 2 months after this operation, the patient had small intestinal obstruction requiring operation from which he recovered, and his present condition is excellent. It seems likely that the intra-abdominal complication after colostomy interfered with small intestinal function and caused the upper gastro-intestinal contents to be shunted into the colon. The later occurrence of actual obstruction fortifies this assumption. The only fatal case in the series (Bancroft) also leaked freely from the colostomy and failed to get relief. Operation was done upon this patient in the belief that further rehabilitation could not be accomplished. The fistula was very large. Resection was difficult because of low lying duodenal ulcer. Death occurred as a result of leakage from the duodenal stump.

These observations enable us to restate our conclusions with slight modifications. It is clear that the typical diarrhea, loss of weight, and deterioration of general condition are commonly due not to gastric or jejunal loss into the colon but to the entrance of feces into the upper gastro-intestinal tract. It is strikingly demonstrated that these symptoms are ordinarily abolished at once by proximal loop colostomy. In a small minority of cases important loss into the colon may occur and may continue after colostomy. As to the cause of this phenomenon, not enough data are available. It is not due to the size of the fistula alone. It occurs too seldom to vitiate the benefits of preliminary colostomy which has other advantages besides.

It is noteworthy that the only death in the series occurred in the only patient in whom rehabilitation could not be effected. This fortifies the opinion already stated that many patients cannot endure the necessary surgery while in their usual depleted condition. All pre-operative measures available should be employed before operation and this applies also to preliminary colostomy or jejunostomy performed in an attempt to improve the condition of an almost inoperable patient. Several such attempts have resulted fatally. Jejunostomy has occasionally helped but in general has failed to improve nutrition. It has no such striking effect as colostomy. The information received shows clearly that there are a considerable number of patients who cannot be rehabilitated so long as the colonic fistula continues to pour its products into the upper gastro-intestinal tract. Some cases reach a state in which even colostomy cannot be withstood. Muller, Allen, Golden, and McKittrick have sent the notes of such cases.

The operation of choice in these patients is subtotal gastric resection. This may be necessary because of conditions at the pylorus but even if the original ulcer seems to have healed experience shows that simple restoration of continuity is followed by reactivation of the ulcer in at least 20 to 25 per cent of the cases. Coller (personal communication) after an experience of 40 per cent mortality appreciated the necessity of rehabilitation by every measure before attempting cure by operation. After this regimen was instituted, 2 patients died, but since that time he has had a remarkable run of 16 operative recoveries with one stage operation. However, only 1 resection was performed. The remainder were simple restorations accompanied in 5 instances by pyloroplasty for stenosis of the pylorus. Already there have been two recurrences of duodenal ulcer. I do not deny that patients who are or can be brought in good general and local condition may be operated upon in one stage by the experienced surgeon with reasonable mortality. Allen's aseptic resection is technically of the highest order but it restores the patient to his ulcer diathesis as already mentioned.

A suggestion of merit in the one stage operation is to avoid the danger of leakage from the repaired or anastomosed colon by bringing the ends out of the incision for later closure in the Mikulicz manner. Both Lee and Joyce relate successful cases done by this plan. That leakage from the repaired or anastomosed colon is a chief danger is a well known surgical fact. It is also known that the best way to prevent such an accident is to defunctionate the colon. This is another advantage of the operation here recommended. There is then no risk in dropping the colon, because it is functionless. Mathewson in his second case actually found by x-ray a small leak which had produced no symptoms. Later, continuity was restored without incident. If a double-barreled colostomy is to be left for later closure, why omit the superior advantages of preliminary colostomy for rehabilitation and greater security in correction of the fistula?

It is proposed, therefore, that the standard treatment for gastrojejunocolic fistula consist of preliminary colostomy to be followed at an appropriate interval by subtotal gastric resection with the necessary repairs or anastomoses to re-establish continuity. A simultaneous jejunostomy by the simple purse-string method may be an advantage. Or in its stead the double lumen tube passed through the anastomosis will insure against distention and afford an avenue for fluids later, if needed. Naturally, parenteral fluids, transfusions as indicated, and careful chemical balance are essential in every case. Ascending colostomy through an oblique loin incision is suggested as answering the purpose and being well away from the field of the second stage. A left rectus or paramedian incision should be made for exploration of the lesion. If conditions seem to favor the one stage radical operation, it may be chosen but the surgeon must remember that he will be working in a field contaminated by infection from the colon. If preliminary colostomy is made, the exploration will at once reveal the site best available and as distant as possible from the field of the second stage. No serious exception can be taken to complete cecostomy or right transverse colostomy. Harvey chose ileostomy but this is less suitable if a considerable interval is to elapse, as it must in depleted patients. Concerning the interval, it is usually a matter of weeks or months before maximum improvement has occurred and the second stage should not be hurried.

SUMMARY AND CONCLUSIONS

In summary then it may fairly be concluded that:

1. The most serious consequences of gastrojejunal fistula arise from admission of colonic contents to the stomach and jejunum rather than from loss of food from stomach through the fistula.

2. Loop colostomy proximal to the fistula is the best means of relieving symptoms and facilitating rehabilitation.

3. Preliminary colostomy permits subsequent correction of the fistula by the necessary radical measures in a clean field and protects the repair of the colon.

4. The operative mortality, 6.6 per cent, is shown to be greatly reduced by this plan.

THE SURGICAL TREATMENT OF ACHALASIA OF THE ESOPHAGUS

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THE term achalasia, applied to the clinical syndrome characterized by dilatation and hypertrophy of the esophagus with non-organic obstruction of the cardia, is employed with the full realization of its pathogenic significance. Numerous other designations such as, cardiospasm, phrenospasm, esophagectasia, megaesophagus, idiopathic dilatation of the esophagus, etc., have been used, clearly reflecting the controversial opinions regarding the etiology of this distressing malady. No attempt will be made here to discuss these various theories as they have been adequately reviewed in previous publications (3, 4, 21, 51, 68, 71, 72). However, we are inclined toward the pathogenic concept which is implied by the term achalasia.

The surgical importance of this condition is not sufficiently realized and has been minimized probably too greatly. Although its incidence is not high it occurs with sufficient frequency to deserve more intensive consideration. Moersch (47) considers it one of the most common diseases of the esophagus. Guisez, in 1935, stated that during the previous 6 years he had examined esophagoscopically 946 patients and of this number 165, or 17.4 per cent, had achalasia. With the exception of carcinoma it was the most frequent cause of esophageal obstruction. This observation has also been made by other investigators (8, 76). Achalasia comprised 17.8 per cent of esophageal lesions in Walton's series. At the Mayo Clinic more than 1200 cases have been observed (16). Undoubtedly in the majority of cases patients can be treated conservatively, but a certain number will require surgical intervention. Of 805 patients treated conservatively by Moersch (48) 71 per cent were completely relieved. However, Walton and Hill were unable to obtain such a high incidence of good results by these more conservative methods. In Wachs' series of 52 cases, 16, or 30.3 per cent, required surgical therapy. Thus, it may be stated that a little less than a third of the cases will not be completely relieved by conservative measures and the majority of these will probably necessitate more radical therapeutic procedures. Whereas every patient should be given the benefit of conservative treatment first, if such measures do not accomplish adequate relief of symptoms in a reasonable period of time surgical intervention should be considered. Undoubtedly in the past there has been too great a recalcitrance on the part of the physician to institute such measures with the result that many patients who could be cured have been permitted to continue having distressing manifestations for years and even to develop irreparable complications. This has been due to some extent to the prevalent impression that the risk of operative therapy is considerably greater than of conservative therapy. Actually, however, the mortality of the latter is only slightly less than the former. In Moersch's (48) series of 804 patients treated conservatively 9 died from splitting of the esophagus, 2 died of starvation, and 12 died at home. Of 239 collected cases in which cardioplasty and esophagogastrostomy were the procedures performed, there were 10, or 4.2 per cent, deaths (51).

The varied procedures that have been advocated and employed in the surgical treatment of achalasia clearly reflect the diversity of opinion and the conflict of views regarding the etiology and pathogenesis of this condition.

In a previous publication reviewing the subject (51) these procedures were classified as follows:

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Presented before the Clinical Congress of the American College of Surgeons, Chicago, October 21-25, 1940.

I. Operations directed at the dilated esophagus
  A. Excision of wall
  B. Esophagoplication
  C. Esophagostomia thoracica
II. Operations directed at the cardia
  A. Dilatation
    1. Retrograde
    2. Transgastric
  B. Plastic
    1. Cardiomyotomy
    2. Cardioplasty
  C. Excision
    1. Cardiectomy
  D. Deviation
    1. Esophagogastrostomy
III. Operations directed at the diaphragm
  A. Phrenotomy
  B. Transposition
IV. Operations directed at the nerve supply
  A. Vagectomy
  B. Sympathectomy

It is considered inexpedient to attempt here a detailed presentation of all these surgical therapeutic measures as they have been adequately reviewed in a previous publication (51). However, it may be desirable to indicate briefly the rationale of these procedures and to describe succinctly their nature. Those having the most rational basis in our opinion will be considered in greater detail.

Based upon the assumption that an artificial reduction in size of the markedly dilated esophagus would correct the condition, Jaffé, in 1897, suggested excision of long strips of the esophageal wall and closure of the resultant defects. This was first performed by Reisinger, 10 years later. Based upon a similar rationale, Meyer (36, 37), in 1911, performed esophagoplication by suturing together two longitudinal folds of the esophageal wall. In addition to this Meyer did a vagolysis. Because of the poor results obtained in 3 cases Meyer (38–40) concluded that a plastic procedure similar to the Heineke-Mikulicz pyloroplasty was preferable. Freeman's procedure, based upon artificial reduction in length rather than width, consisted of exposing the esophagus through a cervical wound and pulling upward on it until the portion below was "rendered quite taut" and then invaginating the upper segment into the lower so that an intussusception was produced. Zaaijer's (81) procedure consisted of gastrostomy and then esophagostomy after preliminary thoracoplasty to bring the chest wall nearer the esophagus. In this way everything the patient swallowed was discharged through the esophageal opening, collected, and then emptied into the stomach through the gastrostomy.

These procedures attacking the dilated esophagus are obviously irrational and at present are of historical interest only. Because the obstruction to the passage of food is apparently at the cardia, operative procedures directed at this structure seem to have a more rational basis. As early as 1882, von Mikulicz (41) had propounded the concept reflected by the term cardiospasm and had drawn the analogy between this and spasm of the anal sphincter associated with a fissure. It seemed logical, therefore, to assume that dilatation of the cardia would be a rational corrective procedure, and, in 1903, von Mikulicz (42–44) performed this operation which consisted of exposing the stomach through a laparotomy incision and introducing into the cardia an instrument resembling a glove stretcher through an incision in the anterior wall of the stomach. In this manner, he was able to stretch the cardia until he could introduce two or three index fingers through it very readily. The procedure was modified by Rotgans who performed the dilatation by forcefully invaginating the anterior wall of the stomach up through the cardia in order to avoid possible peritoneal contamination by opening the stomach. In a previous publication (51) we collected from the literature 80 cases in which patients were treated in this manner. Of this number good results were reported in 70.8 per cent, failures in 10.1 per cent, and deaths in 8.9 per cent. The procedure is obviously not without danger and accomplishes little more than dilatation by the natural oral route.

Mikulicz's view that a true spasm of the cardiac sphincter existed in this condition widely prevailed at the turn of this century. Under this influence, Gottstein, in 1901, proposed extramucous cardiomyotomy similar to the Ramstedt procedure for hypertrophic pyloric stenosis. However, this operation was not performed until 12 years later by Heller. Whereas some (17, 82) subsequently stated that one incision was sufficient Heller emphasized the necessity of two longitudinal in-

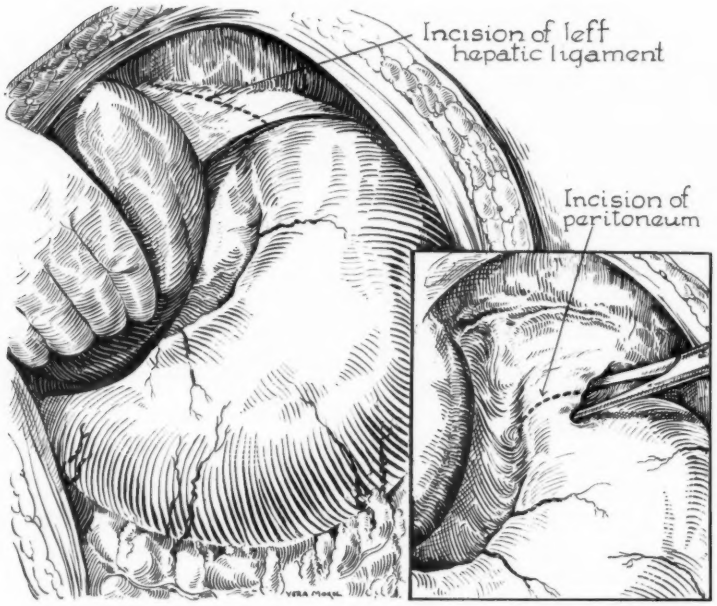

Fig. 1. The technique of esophagogastrostomy in treatment of achalasia which we prefer. Through a high left paramedian or left subcostal incision the left lateral hepatic ligament is exposed and divided. This permits retraction of the left lobe of the liver and better exposure of the cardia. The peritoneum over the esophagus is circumcised at the site of its reflection on the diaphragm as illustrated in the inset.

cisions, one anterior and one posterior. Of 104 cases collected by the authors (51) in which this procedure was done, the results were reported as good in 76.9 per cent, improved in 5.7 per cent, recurrences in 13.4 per cent, and the mortality was 3.8 per cent.

Another plastic procedure first suggested by Marwedel, in 1903, and performed by Wendel, 7 years later, is analogous to the Heineke-Mikulicz (13, 14) pyloroplasty. Whereas this procedure consists of incising longitudinally through the entire wall of the cardia and suturing the defect transversely, the modification proposed by Girard, in 1915, is analogous to the Fredet-Weber (9, 79) type of pyloroplasty and consists of incising longitudinally only down to the mucosa and then suturing the resultant defect transversely. The obvious purpose of the latter procedure is to avoid the opening of the lumen with consequent peritoneal contamination. Of 36 cases collected from the literature in which cardioplasty was performed good results were reported in 93.1 per cent, recurrence in 2.8 per cent, and the mortality was 2.8 per cent (51).

The procedure of excision of the cardia followed by esophagogastrostomy was originally proposed by Rumpel, in 1897, but was not taken seriously until 23 years later when Bier performed the operation in a case reported by Pribam (55). Such a radical procedure is hardly justified in the presence of a benign lesion. In our opinion the procedure deserving the most consideration and based upon the soundest rationale is esophagogastrostomy. This may be performed as a side-to-side anastomosis between the esophagus and stomach thus short-circuiting the cardiac orifice or preferably in a manner similar to the Finney gastroduodenostomy. The former was originally done by Heyrovsky, in 1912, and the latter by Gröndahl, in 1916, although Lambert, in 1913, had accomplished the same end by crushing the spur with forceps. The objec-

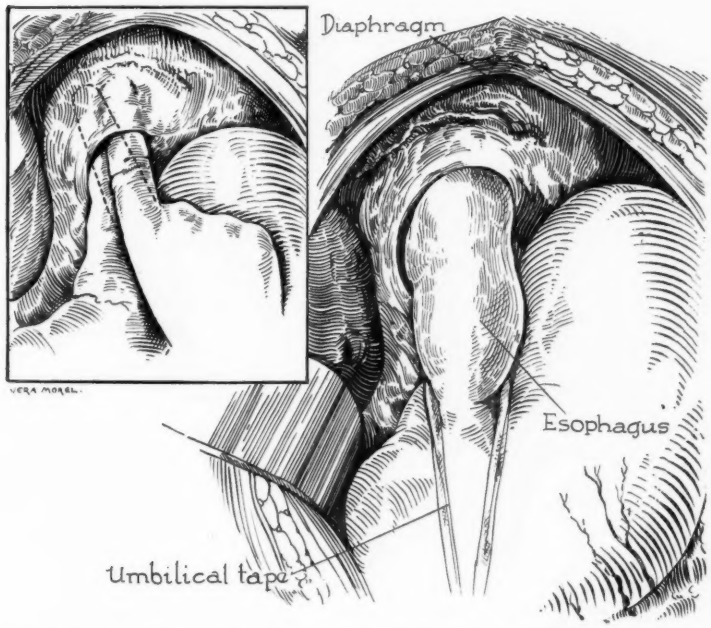

Fig. 2. Esophagogastrostomy continued. A sling of umbilical tape is placed around the esophagus to permit traction downward as it is mobilized from the hiatus by blunt dissection with the finger. In this manner the esophagus is gradually pulled down into the peritoneal cavity for a distance of about 10 centimeters.

tion to the former procedure of side-to-side anastomosis is the presence of a spur which, as emphasized by Frey, may produce some obstruction to the free passage of food from the esophagus into the stomach. In the latter type of anastomosis this cardiac spur is destroyed and a much wider opening is created between the stomach and esophagus thus permitting freer emptying. This method is perferred by us and has been successfully employed in 2 cases previously reported (51). In addition to these we (51) collected from the literature 88 cases in which esophagogastrostomy was done. More recently Wachs has reported 9 other cases making a total of 99 collected cases in which patients were treated in this manner. Of this number 5 died, 1 had a poor result, and the remainder had excellent results. Numerous surgeons have directed attention to a peculiarly interesting feature in the results of this operation as well as some of the other procedures. It has been observed that the functional results following operation are considerably better than the roentgenological studies would indicate. This is exemplified to some extent by one of our patients who, following operation, has remained completely relieved of all previous manifestations Whereas roentgenograms of the esophagus reveal a decrease in size, there is still some dilatation.

The procedure of esophagogastrostomy may be done either through a transabdominal or a transthoracic approach. No attempt will be made here to discuss the various approaches as they have been described and critically analyzed in previous publications (50, 51). In our opinion the transabdominal approach is considered the most desirable and can be done either through a high left paramedian incision or a left subcostal incision paralleling the costal margin. Adequate exposure of the cardia is readily obtained by division of the left lateral hepatic ligament to permit retraction of

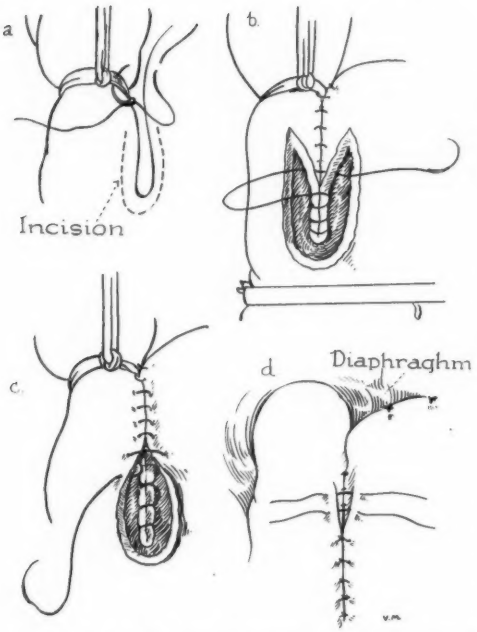

Fig. 3. a, A strip of umbilical tape is tied tightly around the uppermost portion of the mobilized esophagus. This serves a twofold purpose: (1) It prevents spillage from the esophagus above during the anastomosis, and (2) it acts as a means of anchoring the fundus of the stomach to the esophagus by placing the anchor suture around the tape, thus avoiding tearing the friable esophageal wall. b, After the first posterior row of interrupted quilting cotton sutures is placed, an incision is made paralleling this row of sutures, through the stomach and esophagus and carried through the cardia as indicated by the dotted line in, a. The second posterior row of sutures is applied as a continuous through-and-through stitch; No. 00 chromic catgut is used on an atraumatic needle and brought anteriorly as a Connell stitch, c. d, The final row of interrupted Lembert cotton sutures. A few interrupted cotton sutures are used to tack the diaphragm to the esophagus and to the fundus of the stomach in order to avoid traction on the suture line.

the left lobe of the liver as suggested by Lambert (Fig. 1). After the peritoneum is incised over the esophagus at the site of its reflection on the diaphragm, the esophagus is freed circumferentially by sharp and blunt dissection. A sling of umbilical tape is placed around the esophagus to permit traction downward as it is mobilized from the hiatus by blunt dissection with the index finger (Fig. 2). In this manner the esophagus is gradually pulled down into the peritoneal cavity for a distance of about 10 centimeters. A strip of umbilical tape is tied tightly around the uppermost portion of the mobilized esophagus (Fig. 3, a). This excellent technical suggestion of Fromme serves a twofold purpose: (1) it prevents spillage from the esophagus above during the anastomosis, and (2) it is a means of anchoring the fundus of the stomach to the esophagus by placing the anchor suture around the tape, thus avoiding tearing the friable esophageal wall (Fig. 3, a). After the first posterior row of interrupted quilting cotton sutures are placed (52, 53), an incision is made, paralleling this row of sutures, through the stomach and esophagus and carried through the cardia (Fig. 3, a and b). The second posterior row of sutures is applied as a continuous through-and-through stitch, No. 00 chromic catgut on an atraumatic needle being used, and is then brought anteriorly as a Connell stitch (Fig. 3, b and c). This is followed by a final row of interrupted Lembert cotton sutures (Fig. 3, d). A few interrupted cotton sutures are used to tack the diaphragm to the esophagus and to the fundus of the stomach in order to avoid traction on the suture line (Fig. 3, d). The strip of umbilical tape tied around the esophagus is cut and removed. Reinforcement of the anastomotic line by an omental graft as suggested by Palugyay (54) may be done.

Operative procedures directed at the diaphragm are based upon the concept, originally postulated by Sauerbruch and Hacker, that the condition is the result of overactivity, a failure of relaxation, or an inco-ordination of the diaphragmatic crura. This theory is reflected in the term "phrenospasm" proposed by Jackson. On this basis, Bassler, in 1914, suggested division of the diaphragmatic crura. Vampré, who obtained consistently poor results following this procedure, finally concluded that it was irrational. In 1913, von Hacker (20) suggested, in addition to enlarging the diaphragmatic hiatus, drawing the esophagus down and "straightening it out." Because Turner (73, 74) obtained only 1 good result in 5 cases he finally discontinued using this operation.

Surgical procedures directed at the nerve supply of the esophagus in the treatment of achalasia are based upon certain clinical and experimental observations which have been

presented in an attempt to explain the pathogenesis of this condition on the basis of a nervous mechanism. A detailed discussion of these numerous observations which form the basis of this concept is considered inopportune here and the reader interested in this phase of the subject is referred to a previous publication (51). Suffice it to say that in general they may be classified into those incriminating the vagus and those incriminating the sympathetics. Accordingly, the surgical attack has been directed at these respective innervations. Vagotomy was performed by Meyer, in 1911, in addition to esophagoplication but because the results were poor he finally concluded that the procedure was of no value. Similar results were obtained by Sauerbruch (65, 66), Rieder, and Jirasek. Of 11 collected cases in which vagotomy was done, only 1 had a satisfactory result. At present the procedure appears to be of historical significance only.

Probably the first to attack the sympathetics was Récalde (58, 59), who, in 1924, advocated decortication of Auerbach's plexus. He performed this operation on 4 patients and obtained a good result in 3. Ten years later, Knight (28, 29), on the basis of extensive experimental investigations, placed sympathectomy in the treatment of achalasia on a firmer foundation. Performing his experiments on cats because the neuromuscular mechanism of the esophagus in these animals more closely resembles that of humans, he was able to demonstrate the presence of a true sphincter mechanism at the cardia. Moreover, he showed that bilateral vagal section reproduces the clinical and pathological picture of achalasia and that the condition can be relieved by sympathectomy. He also showed that in the human, the sympathetic supply to the cardiac sphincter is derived chiefly from the left side of the celiac plexus and distributed along the left gastric artery. Accordingly he advocated sympathectomy by excision of this artery and the surrounding fat and nervous tissue. Of 5 patients operated upon in this manner by Knight (30, 31) and Adamson, 1 was completely relieved, 1 was considerably improved, and the 3 others showed signs of recurrence. Since then others (6, 35, 64, 69, 70) have reported the use of this treatment but the results in their cases have not been very impressive. A somewhat different technique of sympathectomy was done by Craig, Moersch, and Vinson. These authors reported a good immediate result in a case of achalasia treated by bilateral resection of the cervicothoracic sympathetic ganglia and trunk. We used a similar technique in a case previously reported in which a diagnostic procaine hydrochloride block by the anterior approach (49) was followed by rapid passage of barium through the cardia as determined fluoroscopically. Whereas immediate improvement followed the operation, several weeks later there was complete recurrence. Recently Mitchell stated that the high incidence of failures following sympathectomy may be explained on the basis of the great anatomic variation in the sympathetic supply to the cardia and the consequent difficulty of completely interrupting these pathways.

SUMMARY

1. The surgical significance of achalasia is emphasized. Whereas the majority of patients can be effectively treated by conservative measures, slightly less than a third will require surgical intervention.

2. A number of surgical procedures have been devised and advocated and may be classified in 4 groups: (1) those directed at the dilated esophagus, (2) those directed at the cardia, (3) those directed at the diaphragm, and (4) those directed at the nerve supply.

3. The rationale of these various procedures is indicated briefly and their nature succinctly described.

4. In our opinion the procedure deserving the most consideration and having the soundest rationale is esophagogastrostomy. The preferable technique is described and illustrated.

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SOME FACTORS INFLUENCING THE CURABILITY OF CANCER OF THE STOMACH

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ALMOST recent report on deaths from all causes by the Bureau of the Census shows during the period 1920 to 1938 a steady and inexorable increase from year to year in the percentage of deaths from cancer. This is true of no other cause of death listed. Even diseases of the heart and accidental deaths, while larger in total amount, show a variation from year to year. Cancer of the stomach is one of the most depressing phases of this whole subject and constitutes a large part of the clinical problem of cancer. It comprises 35 per cent of all cancer, causes one-third of all cancer deaths, and results in more than 100 fatalities every day in the year.

The problem is receiving increasing thought as is shown by the ever-growing number of articles written upon the subject, an average of 175 titles annually for the past few years. Thus, an enormous amount of information bearing on the incidence, pathology, treatment, and statistics has been accumulated. It is probable that cancer of the stomach rarely occurs in the normal stomach, and also that the various types of chronic gastritis, atrophic and hyperplastic, are frequent precursors. To speak of irritation alone as a cause is not sufficient unless another factor, susceptibility, which is probably inherited, be added. The chemists have shown the importance of the common factor in the synthetic carcinogenic compounds, the phenanthrene ring system. Among the substances occurring naturally in the body and containing this particular ring system are: ovarian hormone, male hormone, cholesterol, and the bile acids. From one of these, dioxycholic acid, Cook synthesized methylcholanthrene, a strongly carcinogenic agent, and Needham suggests that from normally occurring compounds a deranged metabolism may produce specific carcinogenic substances in the body. There is high estrogenic activity in many synthetic hydrocarbons whose carcinogenic activity has long been known (11) and this may be suggestive in view of the fact that cancer of the stomach occurs most frequently in the male and at the involutionary period. There is much conflict in the literature, the general attitude being one of pessimism and the impression given is that under the present conditions the disease is hopeless for over 95 per cent of its victims. That the situation is not so entirely desperate, however, is revealed by the number of reports of cures of 10 or more years after surgical excision of the growth. In a large number of cases without metastasis 48 per cent were living 5 years after resection (3); and that there are many more who die without the chance of being included in this group is shown by Warwick's study that in 23 per cent death intervened before metastasis occurred. When the neoplasm was still confined to the stomach, 50 per cent of all patients upon whom resection was done were alive 5 years later, and 90 per cent of patients examined 10 years or more after resection were found to be living normal lives (33). The other side of the picture and that which leads to the general pessimistic attitude is drawn by Maes, Boyce, and McFetridge, Saltzstein and Sandweiss, and most recently by Abrahamson and Hinton, who found that out of the total number of cases seen only 4.6 per cent, 7.4 per cent, and 5.4 per cent, respectively, were amenable to surgical treatment. It is very probable that these latter figures closely approximate the true situation for the country at large. There are many other reports equally gloomy and the vast majority of surgeons must admit that they have never seen a cure of gastric cancer in their own practice.

Owens estimates that there are 450,000 persons with cancer now living in the United States. One-third of this great number, or

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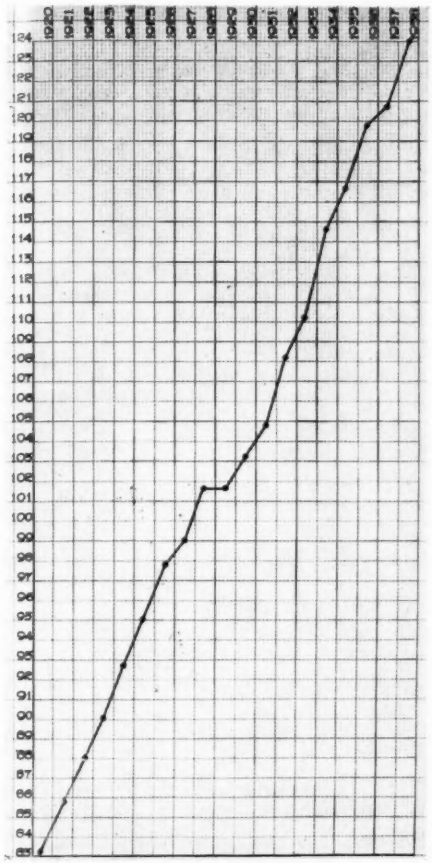

Fig. 1. Cancer death rates. Number per 100,000 estimated population, Bureau of Census 1940, vol. 9, p. 849.

150,000, should approximate the number of cases of gastric cancer. If the average percentage of resectable tumors is 18, there are probably 27,000 resectable gastric cancers in the country at this time. Pack and Livingston estimate the number as in excess of 10,000 and the truth is somewhere between these two figures. The small part of these potentially curable patients who are given their chance for cure is shown by the fact that only 3,000 gastric resections have been reported in the United States during the 50 years of gastric surgery while in the same period 1,500,000 persons have died of the disease (33).

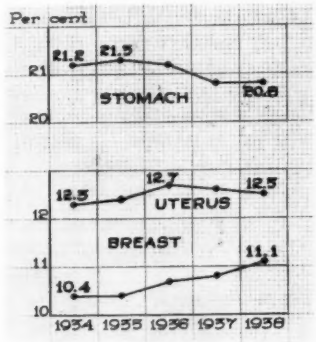

Fig. 2. Death rate per 100,000 estimated population.

It is quite evident that in spite of repeated emphasis placed upon the subject the public is not yet conscious of its serious import, and the profession is not using to the greatest advantage all of the information at its command. The cure of disease ordinarily depends almost entirely on the spontaneous power of the organism to repair itself. Our therapeutic efforts only set the mechanism in motion, and, since natural defenses against the cancer cell are usually not marked in gastric cancer, our therapeutic efforts must be instituted before all power of repair is completely lost. In cancer, as in other diseases, there is an acute and a chronic form, although we are very prone to overlook the possibility of the latter's existence.

We speak of the inoperability of cancer of the stomach after symptoms of a few weeks' duration as though the process dated from the onset of those symptoms, when in reality it is much older. In many cases the consciousness of symptoms comes only after they have repeatedly recurred and gradually become intensified. Limitation of the growth to the stomach does not necessarily mean that it is of recent origin (27). A pre-invasive state may exist for a long time and mild and unrecognized symptoms might be thus explained. The fact that cancer begins in the stomach as a limited disease and may persist thus for a long time has been stressed by MacCarthy, who now thinks that this occurs more frequently than he originally stated. The occurrence of a long history has frequently been noted in

young patients by Friedell. Factors then which influence the curability of the disease are those which make possible the recognition and the prompt surgical treatment of the process during this stage. These factors pertain first to the patient and second to the physician and may be considered under the alliterative headings of: (1) a sensitive patient; (2) a suspicious clinician; (3) a studious and searching roentgenologist and gastroscopist; (4) a superskillful surgeon.

The sensitive patient. It is a fact that most persons consider a mild degree of gastric discomfort to be a part of the normal process of growing older and the words "indigestion" and "dyspepsia" to most minds signify an uncomfortable but entirely benign process. Yet within these two words is the whole story of early gastric cancer symptomatology. It is quite necessary that the public be impressed with the dangerous significance of the symptoms of indigestion and dyspepsia, and while there is some danger of creating a cancer phobia, that in itself would not be an entirely evil thing. Rivers in a study of a large group presenting dyspepsia as the main symptom found up to 14 per cent of carcinoma in females and up to 36 per cent in males from 40 to 70 years of age. In a study of the various reports upon the early symptoms of cancer of the stomach it is noted that there is a predominance of those symptoms which are usually called "indigestion or dyspepsia." Devine describes 12 different forms that this may take. The diagnosis of early cancer of the stomach cannot be made on clinical factors alone, but it is necessary to make a tentative diagnosis based upon an early recognition of symptoms which are suggestive. In order to have these brought to our attention it is necessary that the patient be sensitive enough to notice them and he must be taught that (1) the abrupt onset of dyspepsia in a person who has been well previously, (2) epigastric distress, (3) loss of appetite or a change in food desire, (4) weakness, and (5) an unusual family history of cancer are suggestive and ominous signs which should be reported to us.

Symptoms listed by various authors include those of late as well as those present in early disease.

Gatewood
(13.9 per cent, 58 of 417 resected)

1. Pain
2. *Loss of weight*
3. *Vomiting*
4. Weakness
5. Indigestion and belching
6. Loss of appetite
7. Fullness
8. *Anemia*
9. Regurgitation

Oughterson
(15.8 per cent, 19 of 120 resected)

1. Abdominal discomfort
2. *Loss of weight*
3. Constipation
4. Eructation
5. Anorexia
6. *Vomiting*
7. Regurgitation
8. Diarrhea

Harris

1. Gradually increasing loss of appetite
2. Epigastric distress
3. Indefinite abdominal pain
4. A history of ulcer with change in intensification of symptoms
5. Gradual malaise and fatigue
6. A family history of cancer
7. A little loss of weight
8. *Anemia*

Lahey
(25.7 per cent, 50 of 105 resected)

1. Indigestion
2. Anorexia
3. *Pain*
4. *Weight loss*
5. *Vomiting*
6. Dysphagia
7. Weakness
8. *Hemorrhage*
9. Constipation
10. Diarrhea
11. *Mass*

Ransom and Coller
(13.4 per cent, 56 of 415 resected)

1. Epigastric pain
2. Anorexia
3. *Pain and gas*
4. *Pain and weakness*
5. *Pain and vomiting*
6. Nausea and *vomiting*
7. Stomach trouble
8. Dyspepsia
9. Gas
10. Abdominal distention and dyspnea
11. Nausea and dizziness
12. *Vomiting of blood*
13. Dysphagia
14. *Pain and tumor*
15. *Loss of weight*
16. *Vomiting* and weakness
17. Fainting and pain

Most of these symptoms could be truly called those of simple dyspepsia. Those underlined are not usually due to early disease which was evidently not common in the cases upon which these lists are based, as is seen in the percentage of resectability. The prevalent idea of the symptomatology of the disease is based on more or less advanced cases. If the diagnosis is to be made while the patient is still well, as it must be if we will influence the curability, he will have to be educated to the need of being sensitive to mild degrees of gastric discomfort, and he will fall into one of three classes: (1) those who have never had digestive disturbances before, (2) those who have had previous digestive disturbance due to either organic disease or functional disturbance, or (3) those who have no digestive disturbance but rather complain of some debilitating disease. The patient who is sensitive to mild degrees of digestive discomfort is not the

emaciated, cachectic, and vomiting person who has suffered from pain and increasing distress for from 8 months to a year before seeking medical advice. He is much more likely to be ruddy cheeked, and there are 7 to 8 chances out of 10 that he is a male, with 1 chance in 10 that he is under 40 years of age. There are 8 chances out of 10 that he will fall into the first group, those who have had no previous digestive difficulty. He is not greatly impressed with his symptoms but is much more apt to be annoyed by them. He is really not sick and may have difficulty in describing his complaint being only able to state that he has a "little stomach trouble" whose beginning he can definitely date. He is still able to play 18 holes of golf and notices that there are days when he feels quite well. His central complaint, however, is one of dyspepsia or indigestion or epigastric discomfort. He has lost that sense of well-being following a meal that was once his and its place has been taken by a consciousness of having eaten. He may complain of fullness, a smaller capacity for food, a tendency to eructate, a feeling of motion or of warmth in the epigastrium, and occasionally mild nausea. His discomfort is exactly and vividly described over the radio many times a day and recommendations for symptomatic relief are glibly given. At this time and even later relief may be obtained because these symptoms are apt to be remittent or intermittent. The distress may be intensified by food or it may be relieved by food; it may be worse as the stomach fills or as it empties. The story may exactly simulate that of gastric ulcer as to periodicity and relief by food and alkali as it did in 40 per cent of the cases studied by Jensen and Rivers. The symptoms may mimic the early story of any of the other diseases of the stomach or of any part of the gastrointestinal tract from the esophagus to the colon because early gastric cancer has no typical pattern. One should not expect pain as a symptom; however, it might be advisable to consider the epigastric discomfort, complained of so often, as a type of pain occurring in an organ *ordinarily insensitive*. If the patient falls into the second group—Friedell states that in patients under 30 over 50 per cent have had the symptoms of ulcer for an average duration of 4½ years, while Walters and Walton found this history in 20 per cent—having had this previous digestive trouble, the patient will have grown familiar with its pattern. If he is sensitive he will note with the onset of more serious trouble that there has occurred a change in the degree or rhythm of his symptoms. This is an important fact in the diagnosis of gastric malignancy. Food now tends to increase the pain rather than to relieve it, and there persists a constant mild degree of nausea with occasional vomiting. One cannot, however, depend upon this change, as it may not occur. When it does the patient is apt to be more alarmed than is his physician, and herein lies a danger in that there may be some delay before the cause of the change is thoroughly investigated. The functional dyspeptic, who for years has been uncomfortable but relatively healthy, notices the onset of new and more persistent symptoms—nausea, more or less continued discomfort, and the onset of bad health in place of previous relatively good health. The patient who falls into the third group may note little digestive disturbance, but fatigue and depression are prominent. He suddenly tires easily, is less able to do his work, is more comfortable when reclining, and needs more sleep. He loses interest in his work or in his hobby and is physically unable to carry on without great effort; he has to spur himself to do what he formerly did with zest. This lack of stamina is mental as well as physical. Pernicious anemia may be thought of and treatment on that diagnosis be instituted. This progressive weakness is a prodromal sign in early cancer of the stomach and is due to metabolic changes and the products thereof which are essentially toxic and due also perhaps to some other factors of metabolic disturbance as yet unknown. Having noted these symptoms, so often mild, the sensitive patient is fortunate if he falls into the hands of a suspicious clinician, the second factor influencing the curability of his disease.

It would almost seem that physicians might be divided into two classes: (1) those who are eternally *suspicious* of gastric ulcer and never find it; (2) those who are *never suspicious* of it and eternally miss it. The first are apt to complain of the futility of their efforts, and the

second to comment on the hopelessness of the disease. That physicians lack perception and suspicion, even in their own persons, was shown by Alvarez in a study a few years ago. Fifty per cent of the physician patients studied had had symptoms for at least a year before being treated. The answers to a questionnaire which I sent out to some physicians of my acquaintance are equally revealing.

1. Q. Have you ever had dyspepsia or indigestion?
   A. Often, from very many.
2. Q. Has it recurred or persisted?
   A. Often, from very many.
3. Q. Have you ever taken an antacid without having had a gastric analysis?
   A. Very many had.
4. Q. Have you ever had a gastro-intestinal x-ray series on yourself?
   A. Very few had.
5. Q. Have you ever had a gastric analysis?
   A. Rarely since student days.
6. Q. Do you have a periodic physical examination?
   A. Very many did have.
7. Q. Do you periodically have your heart and blood pressure examined?
   A. Very many did.
8. Q. Do you periodically have your urine examined?
   A. Very many did.
9. Q. Do you consider a gastro-intestinal x-ray series an essential part of a complete physical examination?
   A. Very few did.
10. Q. What are your indications for a gastro-intestinal examination by the x-ray?
    A. Digestive symptoms which persist in spite of adequate medical treatment. Very few considered asthenia, weakness, fatigue or "ordinary dyspepsia" an indication.
11. Q. In what percentage of your patients do you utilize this method of diagnosis?
    A. Many replied "in very few."
12. Q. Why do you not do it in all of your patients?
    A. A few thought it unnecessary as a routine but most said it was a matter of expense.

It seems obvious that a gastro-intestinal roentgenographic study is an essential part of any complete physical examination, and it is almost foolish to be content with investigating the upper and lower few inches of the gastro-intestinal tube and leaving the greater part of it unexplored. As a matter of simple precaution it would seem advisable for every physician at least to have a gastro-intestinal roentgenographic study and a gastric analysis as a part of his personal medical record. It would be interesting to know how many fellows of the American College of Surgeons harbor at the present time the benign precursors of more serious trouble. To the suspicious clinician, be he family physician, gastro-enterologist, or internist the present diagnostic methods are adequate in every way for very many more patients than those to whom they are applied. He knows that in gastric cancer it is always "later than you think." He realizes that any delay in establishing a diagnosis lessens the patient's chance of having applied the only known method of cure—surgical excision. He realizes that most writers stress the need of being suspicious in the patient after 40, but he feels that it would be better to leave out this reference to age and develop the habit of thinking of gastric cancer whenever the dyspeptic syndrome is encountered. He is appalled at the number of patients who treat their own digestive trouble or who are treated without having any searching investigation of its cause, and he knows that there is no such thing as "ordinary dyspepsia" until it has been proved to be nothing more. Quickly aware of the serious possibilities suggested by the sensitive patient's history he makes a tentative diagnosis of carcinoma and proceeds at once to disprove it with all the methods at his command. Physical examination will probably do no more than fail to reveal any other cause for the symptoms. In 70 to 80 per cent free hydrochloric acid is low or absent, but if the acid findings in the gastric secretion are normal or above normal the suspicion will still exist in his mind. Dean Lewis considers achlorhydria to be one of the most valuable early signs, an opinion shared by Holman and Sandusky, who in a recent study state that "low acidity or anacidity remains the single most reliable evidence of carcinoma." Comfort, Butsch, and Eusterman have shown that the acidity is practically always below normal in patients destined to develop carcinoma of the stomach and that this low acidity appears early in all ages and is persistent. Atrophic gastritis seems to be an important cause with secondary degeneration of a chronically inflamed mucous membrane often occurring. The importance of a systematic recheck of patients with achlorhydria and the need of continued suspicion in such cases are imperative. Occult blood in the gastric content and stool is rare in early carcinoma, appearing more constantly in the latter when the disease is further advanced; then it

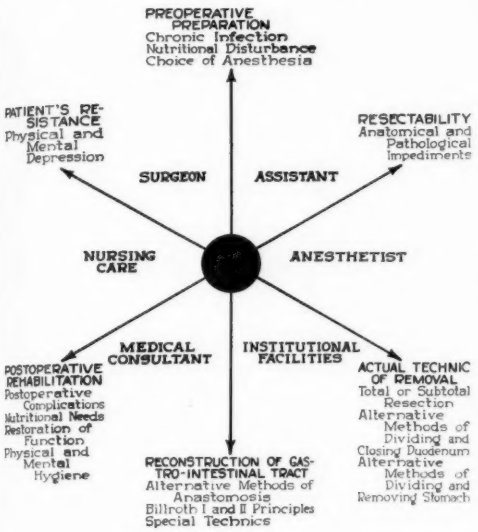

Fig. 3. The surgical problem.

is an evidence of ulceration of the gastrointestinal tract, adds to the suspicion, and should be persistently traced to its source. Devine thinks that slight epigastric rigidity without deep tenderness is highly suggestive when accompanying dyspepsia. As a rule little else is found upon physical examination. If it is, the disease is usually not early and it may be that after having been as thorough as possible the clinician is left with his simple suspicion enhanced only by the added evidence of altered gastric secretion. Persisting in his search he seeks the aid of the roentgenologist and gastroscopist because it is, in the final analysis, by their efforts that the early diagnosis will be established. They must be expert, studious, searching, and persistent. With the attitude of mind that has existed in the past and still exists in many instances, the roentgenologic diagnosis of gastric carcinoma has usually been simply a confirmation of an already made clinical diagnosis and it has usually been easy and late. Christian, writing in 1924, expressed disappointment at the value of the roentgenogram in the detection of early cancer in his experience. In expert hands today it is almost 100 per cent accurate (14). In any other than expert hands it is less than useless. The failure in roentgenographic diagnosis is largely in the case of ulcer carcinoma where after all the problem of differentiation between benign and malignant lesions in some areas of the stomach can be solved only by the pathologist (43, 12). Here the expert roentgenologist will express an opinion only on the physical characteristics of the process. The exact percentage of cancer that occurs in benign ulcer is not of great practical importance if it is appreciated that much gastric ulceration is potentially malignant and should be treated by surgical excision whenever possible. The medical test to determine the nature of an ulcer has two faults: (1) the loss of an interval of time during which the possibility of cure may cease to exist; (2) the fact that partial healing of an ulcer under medical treatment has been noted by the roentgenogram and later proved by resection to be malignant (27). In prepyloric ulcer the possibility of malignancy is so great and in ulceration of the greater curvature it is nearly always so positive that the diagnosis can be made upon the location alone. It is important to stress persistence as a virtue on the part of the roentgenologist because a patient under suspicion must not be lulled into a feeling of security by a single negative roentgenographic report. The examination must be repeated at regular intervals, preferably by the same expert. Negative roentgen-ray findings in the presence of continued symptoms, if accepted as final, may defeat the patient. It would be illuminating to know how many patients fall into the inoperable group after having had a negative roentgenographic report a short time previously. In the presence of suspicious symptoms and of negative roentgenologic findings it is pertinent for the clinician to ask the roentgenologist how he explains the symptoms. This may lead to further and more direct search elucidating the problem. Cole has demonstrated the pathological basis upon which early roentgenologic diagnosis can be made and minor but persistent defects in peristalsis due to infiltration of the submucosa by cancer cells be demonstrated. The lack of pliability he designates as the most delicate of the roentgen-ray findings. The value of many rapidly taken and superimposed films has also been demonstrated by Ledoux-Lebard who shows

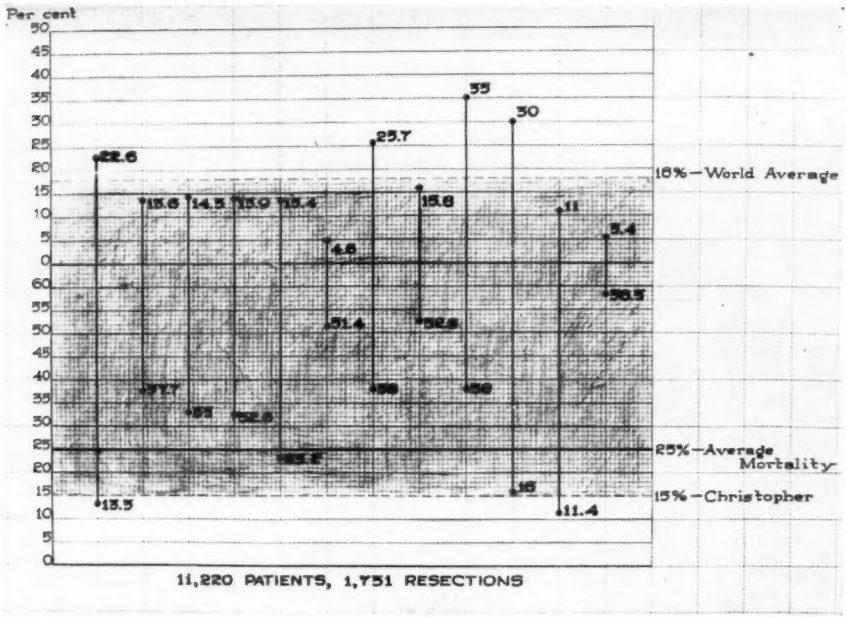

Fig. 4. Relation of operative mortality to resectability. Reports from recent American contributions. Upper figures represent resectability. Lower figures represent operative mortality. Vertical lines connect figures from same series. Shaded area is below the average of resectability and above the average of operative mortality.

their value in the detection of obliteration of the rugae, changes in the mucosal pattern and persistent defects in peristalsis. Gross filling defects due to ulceration or tumor are not due to early disease. The quality of the roentgenogram taken regardless of expense is of the most vital importance to the patient. The question of expense should not be considered when the need and possibilities of benefit are weighing in the balance. In the event of equivocal or doubtful findings by the roentgen-ray or when they are completely negative in suspicious cases, the stomach should be directly inspected by an experienced gastroscopist. Occasionally gastroscopy gives evidence not obtained by any other method and it should be a part of the routine study of the stomach. Its greatest value is in the differential diagnosis of benign and malignant ulcer according to Balfour, but early cancer may be detected during a routine examination. In all cases of achlorhydria it would be valuable to inspect the interior of the stomach and to record the appearance of the mucous membrane for future information, repeating the examination every 6 months to a year. It is in combination with the roentgen-ray, however, and as an adjunct to it that gastroscopy is most useful and its value is again directly proportionate to the skill and the experience of its user. It is not, however, absolutely dependable when taken alone but when its positive evidence is added to doubtful roentgenographic evidence it is of the greatest value.

Having added to the suspicions of the clinician the evidence of the roentgenogram and the gastroscope there remains that last factor in the cure of the patient with gastric cancer, that is, the *superskillful surgeon*. There is probably no other condition in abdominal surgery that demands as high a degree of skill and as wide an experience as does the surgery of gastric cancer. It is here that art and science meet in method. The problem presented to the surgeon is manifold and comprises many elements: (1) An estimation of the patient's

resistance; (2) institution of methods to increase that resistance and safeguard the patient; (3) decision as to the resectability of the tumor; (4) the actual resection of the tumor; (5) the re-establishment of the gastro-intestinal tract; (6) the mental and physical rehabilitation of the patient after operation. The most effective answer to this question demands a wisdom and a knowledge founded upon the widest experience, and to choose the surgeon upon any other basis is to make a grievous and fundamental error. The experienced surgeon knows what he can do, the inexperienced frequently misjudges his capacity. The experienced will consider lesions as resectable in patients who have been refused operation in less experienced hands, and he will be able to carry it to a successful conclusion. Consequently, he who attempts this type of surgery must measure his abilities against the highest standard, and no one should attempt to operate upon a patient with gastric cancer unless he is qualified and intends to resect the growth in the most radical manner. He should be willing to undertake to do this on the basis of expert roentgenologic and gastroscopic opinion alone, realizing that in early cases even the most experienced may be unable to demonstrate any gross pathology by palpation or visualization. Numerous instances have been reported in which the possibility of roentgen-ray diagnosis was demonstrated at a time when the lesion was macroscopically undemonstrable (15).

TABLE I.—RESECTABILITY AND OPERATIVE MORTALITY—RECENT AMERICAN CONTRIBUTIONS

	Total Cases	Resections Per cent	Mortality Per cent
Gray and Balfour	4773	1080, 22.6	13.03
St. John, Whipple, Raiford	718	98, 13.6	37.7
Lewisohn, Mage	647	93, 14.3	33
Gatewood	417	58, 13.9	32.6
Ransom, Coller	415	56, 13.4	23.2
Lahey	195	50, 25.7	38
Parsons and Welsch	691	171, 35	
Maes, Boyce, and McFetridge	758	35, 4.6	51.4
Oughterson	120	19, 15.8	52.6
Maxeiner	60	18, 30	16
Minnes and Geschickter	541		
Pack and Livingston	229	26, 11	11.4
Abrahamson and Hinton	444	24, 5.4	58.3

The experienced surgeon will have in mind primarily the complete removal of the disease and not some preconceived plan of restoring the gastro-intestinal tract. He will, rather, be in command of all of the methods available for restoration and will be able to decide upon and to apply the proper one after removal of the growth, no matter in what condition it has left the gastro-intestinal tract. But to do this he will need great resource and skill and, above all, flexibility of technique. These are qualities which come only with extensive experience so that this type of surgery is not for the occasional operator, the general practitioner surgeon, or the inexperienced. Since it is not given to all surgeons to see many cases of gastric carcinoma or to have the opportunity of operating upon a large series, it is quite imperative that these cases fall into properly trained and competent hands. However, even the greatest skill cannot overcome the handicap of advanced and disseminated disease. The difficulties inherent in the location of some cancers of the stomach are gradually being overcome with perfection of technique. Walters has recently reported only 14.7 per cent mortality in 34 cases of carcinoma at the cardia, and a combined thoracico-abdominal approach may make possible the successful resection of more growths in this area. To stress technique as a cause and statistical evidence of results as the justification of success is not always warranted. However, the study of mortality figures remains the best method of appraisal. The average operative mortality is in the neighborhood of 25 per cent. A select group of surgeons account for one-third of all the resections reported in the last 20 years with an operative mortality of less than 10 per cent. Christopher states that in "skilled hands" the mortality should be less than 15 per cent. That this qualifying phrase does not cover the casual surgeon is shown by the fact that his operative mortality is twice as high as that of the surgeon who is constantly occupied with this problem. This has been conclusively shown by Pack and Livingston who confirm a previous report by Verbrycke on the mortality of the casual surgeon in another and even less difficult field. Ablative surgery is, after all, a crude method of treating this disease but it remains a fact that it is the only successful method so far at hand. Keynes speaking on

the future of surgery prophesied that cancer will eventually be treated by the intravenous injection of a specific. The temptation is great in the face of such a complex problem to build up a hypothesis and to assume that it is an expression of reality. It is more important to cast aside meaningless and useless doubts and to dispel the air of pessimism that exists by attempting more thoroughly and skillfully to utilize what is known until better information is available. In our efforts to use all the factors for success we must create both in the patient and in the physician an appreciation of the dangers of mild digestive symptoms. We must then see that these patients are investigated thoroughly, repeatedly, and expertly, and finally that in treatment only the most expert surgery is offered to them. In the war against this dread and sinister disease it may be that our efforts are simply skirmishes on the margin of the battle, but even if it be so they must be fought with every means at our command and they call for our utmost vigilance and our most persistent effort.

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SULFONAMIDE THERAPY AS AN AID TO SURGERY

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IN this paper an attempt will be made to focus on the problems of surgical infections the knowledge which has been gained through study of the mode of action and the therapeutic limits of the sulfonamide compounds. The term "sulfonamides" is employed to include the three drugs in greatest current use, sulfanilamide, sulfapyridine, and sulfathiazole. I shall not discuss many important details concerning dosage, toxicity, and selection of drugs, for these points are adequately covered in numerous papers in the current literature (2, 8, 12, 17), but I hope to outline the general principles underlying the successful use of the sulfonamide compounds in surgical infections, and to present, very briefly, a hypothesis of the mechanism of the action of sulfonamide compounds which I believe is in conformity with most of the available experimental and clinical data. This hypothesis supplies a theoretical framework upon which a complete scheme of sulfonamide chemotherapy may be constructed.

A WORKING HYPOTHESIS OF THE MODE OF ACTION OF SULFONAMIDE COMPOUNDS

Bacteria produce the pathological processes of infection by reason of their capacity to become parasites in the body. As is the case with all parasites, they obtain their "food" requirements by altering the constituents of the body tissues to suit their own particular needs Bacteria cannot make direct use of large unsplit molecules of protein. The protein molecules of the host must first be broken down into the simpler component amino-acids or polypeptides through the activity of a large number of enzymes, each enzyme being responsible for a certain link in the chemical chain of events. The enzyme completes the particular chemical reaction which it is designed to facilitate when it becomes coupled with the appropriate molecule in its environment. The enzymes must all work together as a team if the supply of energy is to be maintained and if the building stones of new generations of bacteria are to be shaped and fitted together successfully. Failure of any one of the essential enzymes to perform its function properly will disrupt the entire mechanism of bacterial reproduction. It is here that the sulfonamide compounds produce their effects. These compounds bear a close resemblance to certain chemical substances which are essential to bacterial nutrition, of which one, at least, appears to be p-aminobenzoic acid (19) (Fig. 1). Figure 2 shows diagrammatically

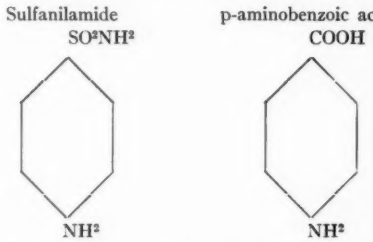

Fig. 1. Structural formulas of sulfanilamide and p-aminobenzoic acid.

how molecules of sulfanilamide may cover up the particular point of molecular reactivity on the bacterial surface, or enzyme, and thereby prevent the proper coupling of p-amino benzoic acid to this enzyme. The effect of this process, called "competitive enzyme inhibition" by the biochemists, is to prevent bacterial utilization of p-aminobenzoic acid, with the result that the cell ceases to divide. Such interference with bacterial reproduction may be termed "bacteriostasis." If there are present on the bacterial surfaces a very large number of enzymes capable of utilizing p-aminobenzoic acid, or if there is an excess of p-aminobenzoic acid in the environment, the number of sulfonamide molecules required to block all of the enzymes and to stop bacterial growth altogether will necessarily be correspondingly

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great. The concentration of sulfonamide required for complete bacteriostasis may be greater than is supplied to the area through the physiological process of drug transport. However, if the molecules of sulfonamide greatly outnumber the molecules of p-aminobenzoic acid, the bacteria cease to multiply, their toxin production stops, and they will die either from "starvation" or by falling prey to the phagocytic cells of the host. When this sequence takes place in the body, the infection no longer spreads into new areas, the bacteria are destroyed, and the patient recovers.

P-aminobenzoic acid is one of a group of substances which perhaps have in common some characteristic chemical configuration, and which act as inhibitors of sulfonamide bacteriostasis. Fildes (3) believes that they are probably "intermediary metabolites" which are essential to the bacteria at some stage in their growth cycle. Sulfonamide inhibitors are present also in peptone (10), and apparently in most enzymatic digests of protein. Pus and necrotic tissue contain large amounts of sulfonamide inhibitors (13). The sulfonamide inhibitors are apparently bound up in the tissue proteins, and are neither available for bacterial utilization nor capable of inhibiting sulfonamide until released through enzymatic degradation of protein. Bacteria which have the capacity of digesting tissue rapidly, such as staphylococci, or bacteria which are in pus or necrotic tissue, are so richly supplied with "sulfonamide inhibitor" substances that they are resistant to the concentrations of sulfonamide compounds ordinarily obtainable within an area of inflammation. There is evidence to indicate that sulfapyridine and sulfathiazole are more effective than sulfanilamide *in vitro* because of the larger amounts of sulfonamide inhibitor required to overcome their bacteriostatic effects. An explanation of the superiority of sulfapyridine and of sulfathiazole over sulfanilamide in staphylococcic infections is thus provided by the work of Woods (19) who showed that it takes five times as much p-aminobenzoic acid to inhibit sulfapyridine action *in vitro* as it takes to inhibit sulfanilamide.

This hypothesis explains the importance of maintaining uniform effective levels of sulfonamide in any patient under treatment by administering the drug at four-hourly intervals; it accounts for differences in the susceptibility of different types of bacteria; it supplies the reason for the great effectiveness of sulfonamide compounds in the treatment of the early stages of acute pleuritis and peritonitis (regardless of the bacterial species involved); and finally, it clarifies the importance of combining timely surgical interference *with* chemotherapy in the management of many different types of infections. The three principal factors which will tend, therefore, to modify the magnitude of the curative effect of sulfonamide compounds in infections may be listed as follows:

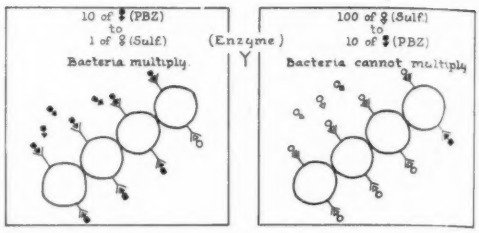

Fig. 2. Diagrammatic representation of competition for enzyme between sulfanilamide and p-aminobenzoic acid.

1. The concentration of the drug maintained in the immediate environment of the bacteria. In some lesions, as in erysipelas, for example, the concentration of drug required to bring about death of all the streptococci appears to be fairly low, perhaps only 1 or 2 milligrams per 100 cubic centimeters. However, in lesions characterized by early necrosis, and the consequent liberation of inhibitor substances, such as in staphylococcic cellulitis, a concentration of even 15 to 20 milligrams per 100 cubic centimeters may succeed only in restricting the spread of the infection to new areas. It is particularly important, therefore, in staphylococcic infections to maintain as high a level of sulfonamide as is compatible with toxic limitations. The amount of drug required for successful treatment of urinary tract infections, due to Escherichia coli, is not great, because sulfonamides are excreted by the kidneys in active form and are present in very high concentration in the urine (5). The prophylactic value of local implantation of sulfa-

nilamide powder in wounds, as reported by Jensen, Johnsrud, and Nelson, is probably a result of the very high local concentration so obtained, a concentration which might be expected to inhibit the growth of almost any type of contaminating bacteria. The local implantation of crystalline sulfonamide compounds into suppurative lesions which have been opened and drained deserves investigation as a possible means of supplementing the limited effectiveness of these drugs in such lesions when they are administered by the systemic routes (17). Furthermore, one should select for treatment in any given case a drug which can be transported to the infected region in adequate concentration. For example, the recent observation by Carey of the limited absorption of sulfathiazole into the spinal fluid is perhaps a contra-indication to the use of this drug in the treatment of meningitis, and suggests the advisability of using sulfapyridine in the treatment of suppurative infections of the meninges. A drug which is highly effective *in vitro* against most of the bacterial species but which is not efficiently transported to serous cavities will perhaps be of less therapeutic value in peritonitis than another drug, having a lower bacteriostatic power but transported in high concentration to the infected area. In the treatment of peritonitis, one should hesitate to substitute a new drug for sulfanilamide until convincing evidence is at hand of the superiority of the new drug within the peritoneum as well as in the test tube. Future progress in chemotherapy may follow the line of developing compounds which will be of value not for any greater specific effect on individual species of bacteria but rather because of special properties of absorption and distribution which cause them to attain high concentrations in infections of certain pathological types or anatomical locations. As an example of progress along this line, Marshall has recently described a new compound (14), sulfanilylguanadine, which is poorly absorbed from the gastro-intestinal tract, but nevertheless is soluble and builds up very high concentrations in intestinal secretions and feces. He reports the occurrence of a very striking reduction in the numbers of Escherichia coli in the intestinal tract following its ingestion. A drug of this type might, as suggested by Marshall, be of especial usefulness in the treatment of enteric infections or in the prevention of peritonitis after colon resections.

2. *The mobilization of the cellular defense.* The anatomical location of an infection, with particular respect to the capacity of the phagocytic defense in the area, is another factor which will tend to modify the magnitude of the curative effect of sulfonamide compounds. The highly developed cellular defense of the peritoneum is probably an important factor in the successful application of sulfonamide therapy in the prevention and treatment of peritonitis due to intestinal bacteria (4, 11, 16). Types of bacteria which are relatively resistant in the test tube to the bacteriostatic action of sulfanilamide are apparently affected by the drug within the peritoneum, at least they appear to be attenuated sufficiently to render them susceptible to destruction by the phagocytes with which peritoneal surfaces and exudates are richly supplied. The Clostridium welchii produces a fatal infection in the peritoneum of the mouse or the rabbit but death can be prevented by sulfonamide therapy (1). However, if the same organism is injected intramuscularly, the drug is quite ineffective (7, 18), and the course of the infection continues to death of the animal. The intestinal streptococci which Meleney believes (15) occur very frequently in symbiosis with Escherichia coli as pathogens in peritonitis of intestinal origin are relatively resistant to the effects of sulfonamide compounds—but our clinical studies suggest that sulfonamide therapy is probably of great value in the prevention and treatment of this disease in humans (11, 16).

3. *The concentration of sulfonamide inhibitor substances.* The final factor of importance in conditioning the curative action of sulfonamide in infections is the amount of "sulfonamide inhibitor" in the infected area. Invasive infections caused by hemolytic streptococci tend in their early stages to spread rapidly through tissues without actually causing necrosis in the infected area. Necrosis develops later if the individual survives long enough to bring about an effort at localization

TABLE I.—EFFECTIVENESS OF SULFONAMIDE IN RELATION TO THE ADJUSTMENT OF FACTORS MODIFYING ITS BACTERIOSTATIC PROPERTIES IN INFECTIONS AT VARIOUS STAGES OF DEVELOPMENT

Stages	Adjustment of factors influencing effectiveness of sulfonamides			Usual effectiveness of sulfonamide treatment	Duration of sulfonamide treatment indicated	Other therapeutic considerations
	Concentration	Phagocytosis	Anti S factors			
I. Contaminated wound, e.g., traumatic wound, colon resection, lobectomy	++ to ++++ (local)	Varies with location	Varies with amount of devitalization	Maximal (Intermediate if thrombophlebitis is present)	Prophylactic treatment for 5–7 days. ?Primary implantation of crystalline sulfonamide	Avoidance of unnecessary trauma. Thorough débridement and irrigation of contaminated wounds
II. Invasive infection, e.g., erysipelas, cellulitis, lymphangitis, streptococcus hemolyticus septicemia, acute pyelitis, acute cystitis, pneumococcic pneumonia	++ to +++	Varies with antibody	Low	Maximal	Continued until 3–4 days after subsidence of infection	Avoidance of surgical intervention. Elevation immobilization and wet dressings to infected part. Administration of specific antibody if available. General supportive treatment.
III. Invasive infection plus localized necrosis, e.g., staphylococcic infections, otogenic meningitis, appendiceal peritonitis, puerperal sepsis	++ to +++	Varies with antibody and location	Peripheral—low Central—high	Maximal at periphery Minimal within zone of necrosis	Continue at least until 3 or 4 days after surgical drainage of the localized area	Drainage or removal of localized area of necrosis after starting sulfonamide treatment. Other considerations as in II
IV. Localized abscesses, e.g., carbuncle, suppurative appendicitis, mastoiditis, chronic staphylococcic infections	+ to ++	Limited	High	Minimal	Drug treatment only an adjunct of surgical drainage. ?repeated local application	Drainage or excision of localized abscess
V. Chronic non-necrotizing suppuration, e.g., gonorrhea, chronic pyelitis and cystitis, chronic hemolytic streptococcic infections	+ to ++++ (local)	Potentially active	Low to intermediate	Intermediate to maximal	Continue for 2 weeks or longer. (Prolonged treatment may be unnecessary in pyelitis)	Surgical intervention usually not necessary except in chronic ulcers which may need débridement. Other agents for local application (e.g. zinc peroxide) may be used in conjunction with sulfonamide

of the infection. However, necrosis of tissue may develop fairly early in the course of staphylococcic infections, due in part to the production of proteolytic enzymes by this organism. Fortunately, the sulfonamide compounds produce their most striking effects in the early invasive stages of these infections, at a time when surgical intervention is of little value. The amount of sulfonamide inhibitor in newly infected tissue or in the blood stream and lymphatics is apparently not great, so that maximal bacteriostatic action of the drug is obtained. After localization and necrosis have occurred, the sulfonamide inhibitors are released, and the sulfonamide has little effect on the suppurative component of the infection, at least when it is administered through the systemic route. Here surgical drainage is of paramount importance. If the abscess is removed or is opened and drained, then the sulfonamide may exercise a bacteriostatic effect on the organisms left in the intact periphery of the lesion, or in the lymph which bathes the wound after necrosis is completed, and final healing may be hastened. In my experience the recovery of patients with staphylococcic septicemia and meningitis has rarely occurred with intensive chemotherapy alone. It is of great importance and contributes largely to the final recovery if possible suppurative foci of localization are attacked surgically without great delay. Patients with staphylococcic septicemia may frequently respond very favorably after 2 or 3 days of intensive treatment with sulfathiazole—their blood cultures may become sterile and they may appear to be well on the road to recovery. However, almost invariably the prolonged continuation of chemotherapy serves only to mask the presence of small localized abscesses which will continue as foci of toxic absorption until they are drained surgically. It now seems to me to be preferable to stop the drug in such cases after about 10 to 14 days of

treatment, so that any foci of localization may develop clinical evidence of their existence. Drug treatment should then be resumed in conjunction with the surgical treatment of these abscesses.

This last factor, involving the amount of sulfonamide inhibitor, appears to me to be the most important of the three which we have discussed. This may be translated into clinical reality in any given case by asking oneself the following question: "How much actual necrosis and digestion of tissue is taking place in this infection?" If the infection may be pictured as a diffuse one, in which the blood supply of the entire infected zone is intact, then one may anticipate a satisfactory result from chemotherapy alone. However, the surgeon must be prepared to remove the gangrenous appendix, or drain the necrotic mastoid, or evacuate the empyema pocket when these or similar complications appear to be present, as the drug alone will not cure these lesions and may serve to endanger the patient through masking their existence.

The chronically draining sinuses which sometimes persist following a suppurative lymphadenitis due to hemolytic streptococci appear to respond well to sulfanilamide therapy alone (9). The rapid disappearance of the organisms from the exudate after institution of drug treatment is probably a result of the fact that this particular exudate does not contain products of continuing tissue digestion, but is composed chiefly of the lymph which bathes the infected area. After the streptococci disappear, the sinuses tend rapidly to close. In chronic infections of this type, particularly those in which the hemolytic streptococcus is present in pure culture, it is advisable to try the effect of a course of sulfanilamide before radical surgery is resorted to. Less should be expected of chemotherapy, however, in the treatment of the chronic suppurative complications of staphylococcic infections.

Many of the principles outlined in this paper are shown in abbreviated form in the accompanying table (Table I). The classification of infections, according to the 5 stages shown, is admittedly only an approximation and some of the rules suggested may need to be changed in the light of further experience.

SUMMARY

1. Sulfonamide compounds produce their effects in infectious lesions by exercising a bacteriostatic effect on the organisms.

2. This bacteriostatic effect is probably a result of a specific interference with the enzymatic utilization by the bacteria of some nutritive chemical factor, such as p-aminobenzoic acid.

3. These substances, the utilization of which is blocked by sulfonamide, will act as inhibitors of sulfonamide effects when they are present in more than minimal concentrations.

4. The curative effects of sulfonamides are maximal when the concentration of the drug is high, when the local cellular defense is active, and when the concentration of sulfonamide inhibitors in the infected area is low.

5. Localized areas of tissue necrosis and abscesses contain large quantities of sulfonamide inhibitor. The organisms within such lesions are protected against the effects of sulfonamides.

6. Surgical treatment of sulfonamide-resistant lesions is of great importance.

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RECENT PROGRESS IN THE SURGICAL TREATMENT OF CARCINOMA OF THE ESOPHAGUS

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PROGRESS in the surgical treatment of carcinoma of the esophagus has not kept pace with that of other thoracic tumors. Torek's (15) successful resection of the thoracic esophagus in 1913 gave rise to considerable interest and hope in the management of this lesion. However, in spite of an abundance of investigative work and many attempts by a large number of surgeons to repeat Torek's accomplishment, only 14 successful resections were reported up to 1934 (3), all of which expired of metastases within 2 years following operation.[1]

This almost uniform failure to respond to therapeutic measures had been due chiefly to three factors: (1) lack of early correct diagnosis (often inexcusable); (2) late development of principles of intrathoracic surgery; and (3) poor response to radiation therapy. The first two of these factors are influenced fundamentally by the pathological characteristics of the tumor.

The onset of the lesion is very insidious, the condition frequently being far advanced before symptoms become manifest. These are usually very mild when first noted and little attention is given them by either the patient or the physician. They may be brought about by the: (1) mechanical obstruction of the passageway by the tumor; (2) influence of the tumor on adjacent structures; or by (3) metastatic lesions.

Although not typical for this condition, dysphagia is the first and most outstanding symptom in the majority of cases. The location of the tumor signifies little in this respect except in the interval between the act of swallowing and the experiencing of a sense of obstruction. By far the majority of the tumors are located in the middle and lower segments of the esophagus, only approximately 10 per cent arising in the upper portion.

Due to its close proximity to other important structures complications caused by direct extension of the tumor are common (about 50 per cent). The first symptoms noted may be from this source, a fact which partially accounts for the variability of the clinical course. The structures most frequently involved include: lung parenchyma, trachea, primary bronchi, pleura, pericardium, blood vessels, and nerves (1).

In addition to the direct influence of the tumor on the wall of the esophagus and neighboring structures, metastases by way of the lymph and blood stream are of primary importance in both diagnosis and treatment. Extension of the tumor in this manner is quite variable; Dormanns reported distance metastases in about 60 per cent of a large series of 1679 collected cases. Occasionally, metastases are widespread and give rise to symptoms before any evidence of the primary growth is manifested.

Spread by way of the lymphatics is most frequent, the lymph flow of the upper two-thirds of the organ being toward the mediastinal, bronchial, and supraclavicular lymph glands, while that of the lower esophagus is directed toward the cardiac glands along the lesser curvature of the stomach. Distant metastases have been reported in almost every organ or structure in the body.

Real progress in the development of intrathoracic surgery has been made only in the past two decades. Prior to this time, alteration of the physiology of thoracic organs during a surgical pneumothorax was not well understood. Thus shock and cardiac failure were common causes of death attending operations on the thoracic esophagus. Infections of the mediastinum and pleural cavity, persistent pneumothorax, pneumonia and hemorrhage were other causes contributing to the

[1]Hedblom's patient committed suicide; Torek's patient lived 13 years and died of pneumonia.

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high mortality of these operations. Thus for obvious reasons treatment of this tumor was relegated to the roentgenologist for several years.

The above described pathological characteristics of this tumor provide ample reason for the poor showing of irradiation therapy. Although some definite effect on the tumor is evident with this type of treatment, destruction of the entire wall of the esophagus by the lesion precludes the establishment of a permanent cure. A report by Watson in 1936 included the results in 666 patients receiving deep x-ray therapy at the Cancer Memorial Hospital in New York City. Of 68 patients receiving the most recent advantages of this therapy, 33 were alive at the time of the report, 8 for 1 year and 2 for 2 years. Of the remainder treated earlier, the average length of life was only 4.8 months.

The recent revival of interest in the surgical treatment of esophageal carcinoma is both timely and deserving. Its importance is more fully appreciated in view of the fact that it is fourth in frequency of all malignant tumors occurring in men over 20 years of age. In a survey compiling 124,827 autopsies from 42 German pathological institutions between 1925 and 1933, Dormanns found it was surpassed in frequency only by cancer of the stomach, lung, and rectum. Of 23,139 deaths due to malignancy in patients over 20 years of age, 8 per cent were due to this tumor.

A major contribution in the recent success enjoyed by surgery in the treatment of this tumor has been by animal experimentation carried out in conjunction with clinical experience. Aided by the establishment of surgical principles especially applicable to this field, and by the improvements of surgical methods, resection of the esophagus in animals was attended by a high degree of success (Miller and Andrus; Saint and Mann; Ohsawa; Adams et al., 2; and Carter et al.). In general the experiments have been divided into two groups, viz.: (1) resection of the esophagus without re-establishing the continuity of the digestive tract; and (2) resection of a segment of lower esophagus with or without a portion of the cardia and reuniting the esophagus and stomach by suture. Various approaches were tried, one through the lower left thoracic wall receiving the most favor. Again, various techniques were used for making the anastomosis.

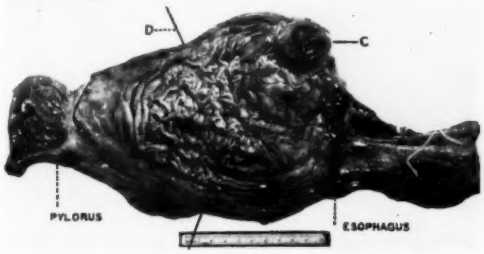

Fig. 1. Photograph of autopsy specimen 3 days following resection of lower end of the thoracic esophagus and gastro-esophagostomy for esophageal carcinoma. There was no leak at the site of anastomosis. The patient, a 60 year old man, died of cardiac failure, cerebral damage, and sepsis. The cardiac end of the stomach was closed by pursestring suture at *C*. The portion of the stomach above *D* remained in the chest following the resection.

Fig. 2. a, left, and b, Microscopic appearance at site of anastomosis seen in Figure 1. Considerable healing has already resulted. *X*, the wall of the stomach; *Y*, the anastomosis; *Z*, the esophagus.

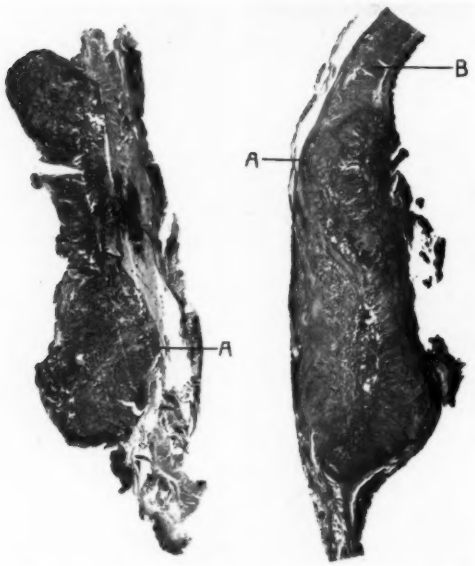

Fig. 3. a, left, and b, Microscopic sections of 2 squamous cell carcinomas of esophagus. Note invasion of entire wall of the organ by the tumor at *A*, thus if destroyed by irradiation no lumen would remain. Resection in each case was followed by an uneventful convalescence. Note marked hypertrophy of muscle of esophagus above tumor at *B* in Fig. 3, b, resulting from obstruction of the passage by the tumor. × 1.3.

In performing these experiments, a number of important factors were recognized:

1. An interrupted two-row suture technique gave the most satisfactory results. Some degree of stenosis at the point of anastomosis resulted when a continuous suture was used. Thus the anastomosis was made similar to that of an end-to-side entero-enterostomy with the exception that interrupted sutures are used instead of a continuous suture.

2. Tension on the suture line of the anastomosis was one of the major causes of its failure to remain intact. This could be obviated by drawing enough stomach into the thorax to obtain complete relaxation at the point of the anastomosis. Stay sutures on either side of the anastomosis may also be of value in relieving tension. When any considerable degree of tension was present, leakage from necrosis at the line of suture could be expected.

3. Postoperative mediastinitis and pleuritis due to contamination at the time of operation was minimized by careful walling-off about the field of operation. An end-to-side type of anastomosis rather than an end-to-end union decreased the likelihood of contamination. For this reason the lower end of the esophagus or the cardiac end of the stomach was closed and the fundus of the stomach used for anastomosis with the upper end of the esophagus.

4. Trauma to the vagi should be avoided during the mobilization of the esophagus. Much more postoperative vomiting was observed when the vagi were unduly traumatized or divided during the resection.

5. Mobilization should include only that part of the esophagus to be resected, thus interfering with as little as possible of the blood supply to the cut end of the esophagus to be used for the anastomosis. Aseptic necrosis with resultant leak at the site of the anastomosis was much less likely to occur when this was observed.

CLINICAL APPLICATION

Pre-operative preparation of the patient. This is an important factor and has contributed much to the success of the operation. Since many of these patients are both dehydrated and undernourished when first observed, normal saline solution alternating with 5 per cent dextrose solution administered intravenously is advisable for a few days preceding operation. In cases in which obstruction is less severe a high caloric liquid diet will improve the patient's general condition. The blood count is usually lowered and a transfusion is advisable. In some cases a preliminary jejunostomy may be desirable.

Anesthesia. The choice of anesthesia is very important (8, 10). Great stress has been placed by some authors on the necessity of intratracheal positive pressure anesthesia for intrathoracic operations. The importance of this type of anesthesia in some instances is not to be denied. It has also undoubtedly given surgeons a sense of security in the carrying out of intrathoracic operations. It has long since been known, however, that most intrathoracic operations may be performed,

and some with greater ease, under simple mask gas-oxygen (particularly ethylene or cyclopropane-oxygen) inhalation anesthesia under slight positive pressure; the pressure obtained thereby being ample for maintaining inflation of the lungs for the necessary gas exchange. It also allows for sufficient relaxation of the lung to give adequate exposure for carrying out the operative procedures, a factor which cannot be overemphasized. The danger of introducing mouth organisms into the tracheobronchial tree during intrabronchial intubation with resultant postoperative pneumonia has been discussed by some (Rienhoff) authors and it is a factor to be kept in mind. Ohsawa has emphasized the value of free open thoracotomy for operations on the thoracic esophagus because of better exposure with relaxation of the lung. We have used simple mask ethylene-oxygen anesthesia for various intrathoracic operations and have found it to be entirely satisfactory. When the operation is completed the remaining surgical pneumothorax is obliterated by aspiration of the air through a catheter drain rather than by distention of the lung with a high positive pressure.

Prevention of infection. Since infection is one of the major hazards of this operation every precaution should be taken not only to prevent contamination of the pleural cavity or mediastinum but of the chest wall as well. Complete walling-off with warm moist sponge pads will prevent gross contamination during the resection and resuture when an anastomosis is made. The contents of the esophagus are prevented from spilling into the field either by the use of a small sponge inserted into its lumen, by a fairly loose tie of tape just above the upper cut end of the esophagus, or by the application of a very soft clamp. The latter two are more satisfactory since they prevent constant oozing of blood which tends to obscure the field. Soiling is less apt to occur when an end-to-side anastomosis between the esophagus and the fundus of the stomach is used. In this respect attention must be called to the blood supply of the esophagus and the stomach. Necrosis of the fundus of the stomach following ligation of the coronary sinister artery of the lesser curvature has been reported by Kirschner and others. Ohsawa has also emphasized this danger. However, the results of our experiments and experiences of American surgeons have not substantiated these earlier observations.

TABLE I.—SUCCESSFUL RESECTION OF ESOPHAGUS FOR CARCINOMA

Period	Cases	Remarks
Before 1934	14	All patients except Torek's died within 2 years after operation. His patient lived 13 years, dying of pneumonia
1934–1938	15	
1938–	34	20 living, some up to 4 years, = 58+ per cent. About 50 per cent of 68 operations were successful

Relative recent advancement in the surgical management of this tumor.

When no anastomosis is made, protection of the upper cut end of the esophagus by a rubber cot will help to minimize contamination of the mediastinum when the upper segment is drawn up through a low cervical incision.

Operation. To von Mikulicz, Sauerbruch, Zaaiger, Torek, and Lilienthal (13, 14) much credit is due for the development of the operative treatment of carcinoma of the esophagus. Although a large variety of operations have been devised, only two have been extensively employed with success. For tumors located in the middle and upper portions of the esophagus, the operation developed and used by Torek in the first successful resection in 1913 has remained the procedure of choice. This entails the division of the esophagus below the site of the tumor, inversion of the lower end by pursestring sutures and drawing the upper end with the tumor out through a low cervical incision. This is connected with a gastrostomy tube sometime later, thus enabling the patient to eat and to swallow his food through the artificial esophagus.

The second type of operation is employed when the tumor is located in the lower portion of the organ. Following the resection of that portion of esophagus involved by the tumor along with a portion of the cardia in some cases, the fundus of the stomach is brought into the thorax through an opening in the diaphragm and united with the esophagus by suture. Thus the continuity of the digestive tract is re-

TABLE II.—COMPARISON OF RESULTS OF TWO TYPES OF OPERATIONS (1938–1940)

Surgeon or clinic	Operation*		Successful cases		Length of survival	Cause of death	Now living Duration
	A c̄ anas.	B s̄ anas.	A c̄ anas.	B s̄ anas.			
Alexander		3		1			B. 14 mos.
Bird	1	2	1		A—6 mos.	Diabetic coma (liver metas.)	
Carter	2	2	2	2	A—10 mos. B—6 wks.	Stricture Meningitis (empyema)	A. 18 mos. B. 18 mos.
Churchill	5		1	2			A. 1 B. 2
Eggars	4	10	0	4 (2 reported)	B—7 mos. B—7.5 mos. B—18 mos.	Metastases Metastases Metastases	B. 5 mos.
Garlock	4	10	2	7	B—22 mos. B—1+ yrs. B—1+ yrs. B—3½ mos.	Recurrence Recurrence Metastases Coronary disease	A. 1 yr. A. 17 mos. B. 3.5 mos. B. 8 mos. B. 4 yrs.
Marshall	1?		1				A. 8+ mos.
Ochsner	2	2	1				A. 1+ yrs.
Overholt	2	2	2		A—1 yr.	Metastases	A. 2 mos.
Scott		1?		1			B. 1+ yrs.
University of California	4	4	1	3 (1 reported)	A—1 mo. B—1 mo.	Metastases Chylothorax	A. 10 mos. B. 3 mos.
University of Chicago	2	4	1	2	B—1 yr.	Metastases or recurrence	A. 2 yrs. 9 mos. B. 8 mos.
Total	67		12+ + 22=34 32/65=49+%				A. 9 + B. 11 = 20 20/34 = 58 +%

*c̄ anas. = with anastomosis s̄ anas. = without anastomosis

Although the Torek operations double the number of the anastomosis, the number living at present was about equal. The mortality was approximately the same for each — 50 per cent.

established. The approach for the second type of operation is made through the lower chest wall (seventh rib bed) on the left side. This site may also be used for the first type and has the advantages over the right side approach in that either operation may be decided on after the lesion is exposed and also that glands at the lesser curvature may be resected through an opening in the diaphragm.

Postoperative management. This should include maintenance of adequate water and mineral balance and for the first week following operation fluids should be administered intravenously and subcutaneously. A blood transfusion as a routine both during and immediately following operation will help to prevent shock and will hasten convalescence. Oxygen therapy is indicated in the presence of cardiac embarrassment. In those cases in which there is re-establishment of the continuity of the digestive tract, nothing by mouth is advisable for at least 4 to 5 days during which time fluids and nourishment are given through a jejunostomy tube or by intravenous administration. (Garlock has dispensed with gastrostomy or jejunostomy successfully.) Continuous siphon drainage applied to a stab wound drain of the pleural cavity will not only prevent an accumulation of exudate but will maintain the lungs in complete expansion, both of which are requisites for rapid healing and a smooth postoperative course. The siphonage need not be more than 25 to 30 centimeters of water and may be easily obtained by the use of a double Wangensteen apparatus.

The recent advance in the surgical treatment of this tumor brought about by investigative studies and advanced clinical methods is strikingly demonstrated in the following statistics: Whereas only 14 successful resections were reported up to 1934, during

the next 4 years 15 cases were recorded and 34 more have been collected from reports and personal communications since 1938. This latter number is far from complete since correspondence was carried out with only 40 American surgeons and with no surgeons from foreign countries. The 34 successful resections were made from 68 operations by 12 surgeons, thus an operative mortality of 50 per cent. Of the 34 cases 20 or 58+ per cent are now living as long as 4 years following operation.

It is interesting to note that resection of an esophageal carcinoma accompanied by gastroesophagostomy carries no more risk than resection of the thoracic esophagus alone. Since approximately 45 per cent of the tumors are located in the lower one-third of the esophagus, re-establishment of the continuity of the digestive tract is possible in a large percentage of cases without additional risk.

This report is being made without undue optimism. Although definite progress has been effected much remains to be desired. For a tumor ranking so high in incidence, many more operable cases should be receiving proper therapy. According to Watson 300 people die of cancer of the esophagus each year (3.5 per cent of all cancer deaths) in New York City. Other cities report even higher percentages. The United States vital statistics for 1938 record 4,871 deaths in Chicago due to cancer and other malignant tumors. About 5 per cent or 245 deaths would represent those due to esophageal carcinoma.

Diagnosis is usually not difficult when once the tumor is suspected. Dysphagia in patients over 35 years of age is due to cancer of the esophagus in a high percentage of cases and must be treated as such until proved otherwise. Fluoroscopic and roentgenological examination following the ingestion of barium will demonstrate evidence of obstruction in the presence of tumor. Esophagoscopy and biopsy of the obstructed region will lead to a correct diagnosis. Before real progress in the cure of this lesion can be effected it is essential that the profession as well as the laity be educated as to the high incidence of the lesion, the need for early diagnosis, and the fact that successful surgical treatment is possible.

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TREATMENT OF TRAUMAS OF SKIN AND SUBCUTANEOUS TISSUES

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IT has been said that beauty is only skin deep. This statement may be true in individuals who have not suffered trauma, but when trauma has occurred beauty or loss of beauty of the skin depends largely on the repair of the subcutaneous soft parts and occasionally of the underlying osseous structures. The loss of beauty in old age is in part due to the atrophy of the fat and connective tissues.

I have become convinced that many of our failures in the treatment of acute traumas of the skin and soft parts are due to lack of appreciation of the pathology occurring in the subcutaneous fat and connective tissues. I desire, therefore, to present certain types of failures and to suggest methods of treatment that will improve the end-results. To facilitate the discussion the following types of traumas will be presented: (1) severe contusions of the skin and soft parts; (2) lacerated wounds of the skin, presenting a consideration of primary and delayed primary closure; (3) avulsion wounds of the skin and subcutaneous tissue; (4) lacerated tendons, presenting the criteria for immediate and late suture.

The following examples are illustrative of the types of failure due to the initial treatment in injuries of the skin and subcutaneous tissues. It is relative to these failures that I desire to present some of the later advances in surgical therapy.

We have all treated lacerated wounds after what seemed to us satisfactory débridement and suture and have been alarmed at the onset of rapid infection with loss of tissue beneath, the delay in healing, or, occasionally, a more tragic end.

Another type of case which we have all seen, for example, is illustrated by a patient admitted to the City Hospital of New York with an avulsion injury of the thigh immediately above the knee. The skin and soft tissues had been rolled downward, as a stocking. Despite careful cleansing, débridement, and loose suture, infection and gangrene of the skin resulted.

All of us have seen avulsion injuries of the dorsum of the hand and foot, in which gangrene of the skin has resulted despite careful toilet and suture.

Tendons united with extreme care often apparently heal and the patient is discharged from the hospital, but we learn on follow-up that in the meantime the wounds have opened and that pieces of necrotic tendon have been extruded.

As the common failures have been listed, it is in order to approach each type of injury from our knowledge of the pathology involved, and to present improved methods of therapy.

CONTUSED WOUNDS

The success or failure of the general treatment of contused wounds of the skin depends largely on tissue tension. If an artery, even of relatively small size, is ruptured during the injury, the extravasation of blood into the tissues increases the tissue tension, producing thrombosis of the veins, thus leaving the tissues susceptible to infection.

Severe contused wounds which produce hemorrhage beneath the surface should be carefully watched. In severe contusions, Babcock advises releasing incisions down through fascia on each side of the injury, in order to relieve tension and allow the extravasation of the collected serum. In cases in which the trauma is not as severe as he has described, the aspiration of the hematoma beneath the skin may be sufficient. Such wounds demand surgical judgment and excellent operative technique. If one hesitates when necrosis is beginning, one may lose large areas of tissue. If the patient is seen early and is in a satisfactory condition, small and deeply contused

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wounds may be treated by excision of the traumatized area and primary suture.

LACERATED WOUNDS

The treatment of lacerated wounds of the skin and subcutaneous tissues is dependent on: first, the age and general condition of the patient; second, the condition of the skin at the time of injury; third, the type and cleanliness of the instrument producing the injury; and, fourth, the length of time elapsing from injury to operation. While these conditions are elementary and generally known, they are not always given the attention they deserve.

1. *The age and condition of the patient.* It is advisable in obtaining the history to get the patient's reaction to previous traumas. There are some patients who, despite severe injuries in the past, have been resistant to infection, and it is logical to assume that they may be resistant in the present emergency. Others have shown susceptibility to infection and must be treated in a much more conservative manner.

2. *The condition of the skin.* Whether the skin is clean or dirty at the time of injury and also the location of the injury are important factors in our consideration of treatment of soft parts. Braine, in his discussion of primary suture, states that buttock wounds and wounds of the leg should not be treated by primary suture, as they are more susceptible to infection, due to location and blood supply. The wounds over the tibia are obviously slow of healing and need careful watching.

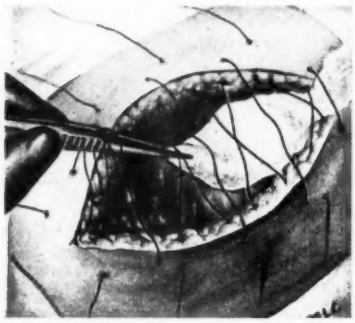
3. *The instrument.* The type of instrument producing the injury is important, as a sharp instrument causes less surrounding tissue trauma than a blunt one, which creates necrosis and hemorrhage of the deeper connective tissue structures, as well as lacerations of the skin.

4. *The lapse of time.* The length of time elapsing from injury to operation is of significance. Bruning quotes the well known experiment of Friedrich showing that there is a lag period in bacterial growth for about 6 hours. During this period the wound may be excised with little fear of bacterial spread. After this time the bacterial growth is so increased that it is difficult to obtain by débridement a relatively clean field.

The present trend in surgery in preparing a contused or lacerated wound for treatment is to avoid, in so far as possible, the active antiseptic, as it is felt that an antiseptic strong enough to kill bacteria is also apt to destroy the resistance of the living cells of the host. Many writers advise the careful washing of the wound, followed by the use of antiseptics on the neighboring skin. There are others, however, who believe that simple washing, with white soap and water for many minutes is sufficient. The author favors the method of copious gentle washing of the wound with soap and water. The wound is then protected by gauze dressing, after which the skin is prepared by cleansing with soap, water, ether, and alcohol, and the wound is again lavaged.

The foreign literature, and particularly the French literature, of the present war concerns itself especially with a discussion of primary versus delayed primary suture in lacerated wounds. While this problem has not arisen so much in civil surgery, nevertheless it is of vital import and it might be well to review some of the opinions that are expressed today. Braine, in an article on primary suture of war wounds, summarizes the situation as follows. He states that "primary closure is contraindicated when the circumstances are not ideal, when the wound is not recent, when the surgical equipment is imperfect, when the operator is not experienced, and when the injured cannot be closely followed for at least 2 weeks." He presents the following general instructions:

> "All primary sutures entail a certain risk and should never be lightly performed. They should not be done as a routine measure—each case should be considered on its merits. Suture should not be performed unless all conditions are favorable as regards the wounds, patient, surgeon's experience, and the military situation. Primary suture following excision is always a delicate operation upon which the patient's life may depend. Suture is not indispensable to save the patient's life; on the contrary, it may result in fatal accidents. Every unsuccessful suture aggravates the original condition. Meticulous excision of the wounded area, and not the suture itself, is the essential feature. The suture may be performed later at leisure with a greater margin of



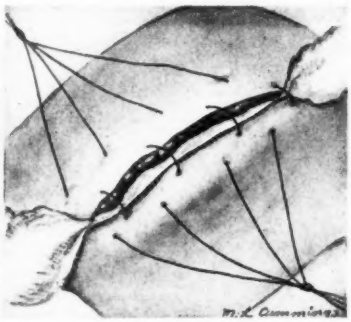


Fig. 1, left. Acriflavine pack being placed in wound. (Courtesy of Coller and Valk, *Ann. Surg.*, 1940, 112: 260.)

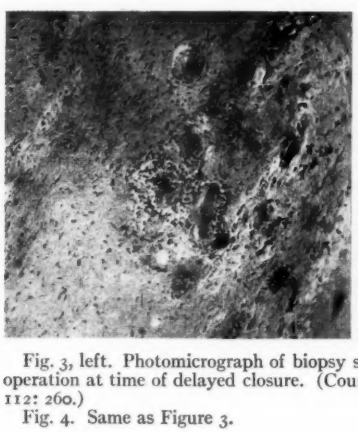
Fig. 2. Acriflavine pack in place. (Courtesy of Coller and Valk, *Ann. Surg.*, 1940, 112: 260.)

safety. Excision followed by suture is a procedure of patience, care, and thoroughness. The wound should be scrupulously examined before the tissues are approximated. In doubtful cases it is better to apply dressings and drains. Primary sutures require careful watching up to complete cicatrization, and the surgeon must be prepared at any moment to remove the sutures. The small extent of the surface injury may not be an indication of the amount of deeper injury, which should always be determined. Primary suture without drainage is exceptional in wounds of the buttocks, thigh, and calf. Primary delayed or secondary suture is worthy of increased attention; although the results are less brilliant the method is safer."

Bruning states that the most important feature in after-treatment is immobilization, which should be carried out as in the case of a fracture, in order to prevent any displacement of the tissues in relationship to one another.

Gregoire, Chevassu, Lenormant, Gosset, and Roux-Berger all warn of the damages of primary suture in war wounds. While they admit that the few spectacular cases make one attempt to utilize the procedure, the failures more than militate against these successes.

In this country, Coller has recently presented a very interesting series of cases of potentially contaminated wounds which he has treated by delayed primary suture. His discussion is largely one relative to the possible infection of abdominal wounds from contamination beneath the surface, but the surgical principles are the same as one finds in lacerated wounds. Coller says:



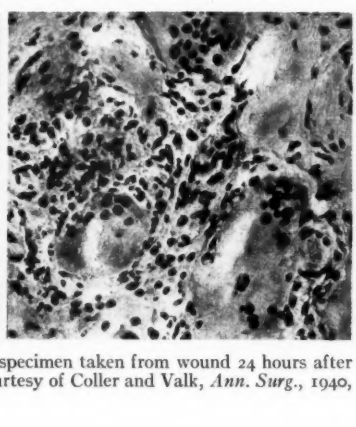


Fig. 3, left. Photomicrograph of biopsy specimen taken from wound 24 hours after operation at time of delayed closure. (Courtesy of Coller and Valk, *Ann. Surg.*, 1940, 112: 260.)

Fig. 4. Same as Figure 3.

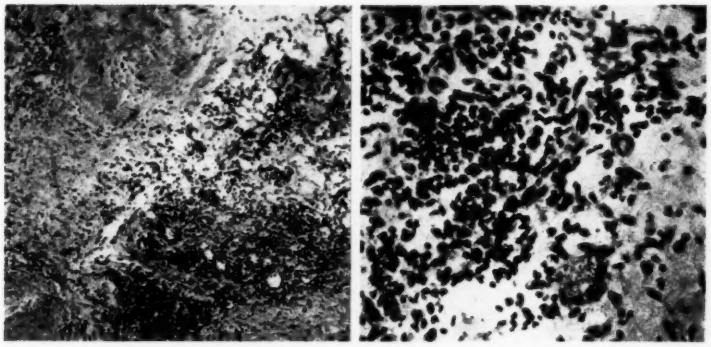


Fig. 5, left. Photomicrograph of biopsy specimen taken from wound surface 48 hours after operation at time of delayed closure. (Courtesy of Coller and Valk, *Ann. Surg.*, 1940, 112: 260.)
Fig. 6. Same as Figure 5.

"Fraser, in 1918, reported an incidence of 9.7 per cent failure in 41 cases of primary closure as compared with 4.5 per cent failure in 63 cases of delayed primary suture. He also reported 31 bacteriologically negative wounds from 35 contaminated wounds after 48 hours' treatment by delayed primary closure employing a flavine pack in the wound. In 1918 delayed primary closure of all soft-tissue wounds, excepting those in the scalp, face, and hands, was advised by the surgeons of the American Expeditionary Force. The best results were obtained when the wounds were closed within 50 hours."

Coller's method is to suture loosely the muscles and fascia beneath the fat and the skin. After careful cleansing and débridement of the fat and subcutaneous tissues, fine silk sutures are inserted in the skin but left untied, and the wound is packed from each end with acriflavine gauze down to the fascia. In 24 to 48 hours the pack is removed and the sutures are tied. He presents a series of 21 cases treated in this manner, with only 1 minor infection. I have had the opportunity of using this method 8 times successfully. Coller presents microscopic sections of the wound edges in 24 hours and states that the sections show a residue which consists of fibrin, in the meshes of which are polymorphonuclear leucocytes, wandering cells, some necrotic tissue, and many fibroblasts (Figs. 1–6). As cultures taken from the wound at the time of operation and at the time of closure do not show destruction of the bacteria by this method, it must mean that two important surgical principles are involved: (1) the release of tension in the wound by leaving it wide open; and (2) the stimulation of the reparative process of the wound or the creation of bacteriostasis by the presence of gauze soaked in acriflavine. He believes that after the coagulation of the fibrin the resistance of the wound is greatly increased because of the sealing off of the capillary and lymph spaces, which tends to keep infection localized or below the clinical horizon.

In discussing the paper of Coller, McClure suggested that part of the success of this method might be due to the inhibitory effect of the air upon the growth of anaerobic organisms, as well as its bacteriostatic effect on the aerobic bacteria.

One might summarize the problem of primary or secondary closure of lacerated wounds as follows: Primary closure may be attempted if the patient is healthy, the skin clean, the instrument creating the damage relatively clean and sharp, and if the patient is seen well under 6 hours after the injury. The surgeon performing the operation must use meticulous care in lavaging the wound and in gentle excision of all traumatized areas. Sutures must be inserted in order to avoid dead spaces, but with care that there shall not be tension when the secondary edema occurs following the operative procedure. Plaster encasement or adequate splinting should be utilized to prevent muscle pull and production of hematomas. Delayed primary suture should be performed in the event that the aforementioned criteria are not present.

Fig. 7. Immediate postoperative appearance. The fenestrated, immobilized plaster encasement was necessary because of a fracture. (Courtesy of Farmer, *Ann. Surg.*, 1939, 110: 952.)

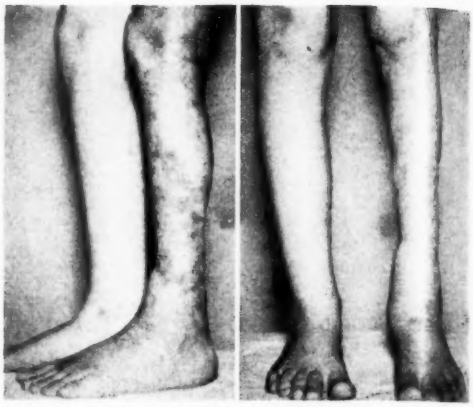


Fig. 8. Front and side views of final result. (Courtesy of Farmer, *Ann. Surg.*, 1939, 110: 952.)

It is obvious that there is a third type of injury which I have not mentioned because it seems evident to me that one would not attempt either primary or delayed primary suture; that is, the type of injury in which there is extensive tissue damage and in which it is evident that the wound must be débrided and left wide open for healing by granulation. In this type, immobilization of the neighboring joints is often a necessity in order to prevent constant trauma by muscular action. Because of its severity, the lesion may need various therapeutic measures. Dakinization or vaseline gauze packing, as by the Orr method, may be the therapy of choice. Early skin grafting is advisable as soon as the granulations permit.

AVULSED WOUNDS OF THE EXTREMITIES

Farmer has postulated what seems to the author to be an adequate theory of the cause of failure in avulsed wounds. He states that when the skin and subcutaneous fat are avulsed, thrombosis of the venous and lymphatic vessels is produced by the trauma. On the other hand, the arterial vessels are not as easily injured, and they continue to pump blood into the traumatized zone. When the pressure of the incoming blood overcomes the normal tissue pressure, necrosis occurs as the smaller arteries begin to thrombose. We are accustomed to see a similar pathological process in the pregangrenous stage of acute cholecystitis. All surgeons are conversant with the appearance of the bluish gall bladder which is swollen and edematous and which one is apt to call beginning gangrene. Sections of such gall bladders, however, show the tissue full of extravasated blood. The initial process has probably been a venous occlusion due to pressure of an impacted stone in the cystic duct. As the tissue pressure increases, the artery gradually becomes thrombosed and then, and not until then, does active gangrene occur. Fortunately for the gall bladder omental adhesions are apt to bring relief from some of the tissue tension.

If Farmer's theory is true, his method of treatment is a real advance in the handling of avulsed wounds. He believes in the excision of all of the avulsed skin, for he says that if a portion of the skin is left attached the arteries will continue to pump blood into the skin and subcutaneous tissue and gangrene will result. When the skin has been removed, the assistant carefully débrides the underlying structures, removing all dead or traumatized tissue. Farmer advises the cleansing of the raw area with aseptic rather than antiseptic fluids. Thus soap and water and saline are the solutions of common choice. The surgeon removes

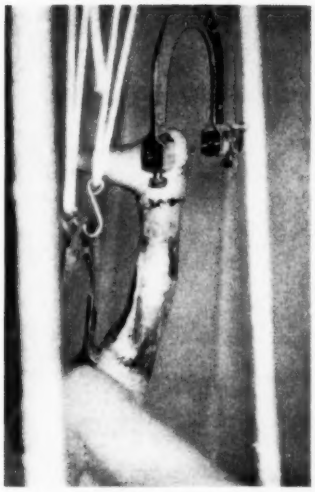


Fig. 9. The result 2 weeks after accident. (Courtesy of Farmer, *Ann. Surg.*, 1939, 110: 952.)

the avulsed skin. It is held on a firm flat surface and the fat is removed by scraping or by cutting with curved scissors well into the dermis. After the combined procedure of débridement of the deeper structures with complete hemostasis and excision of the subcutaneous fat, the skin is then sutured accurately into the defect from which it was removed. To prevent dead spaces, quilting sutures are used in addition to the circumferential sutures, and the graft is perforated with numerous small stab wounds. The primary dressing is of normal saline. Firm pressure is obtained by bandaging, and a plaster encasement insures immobility. The dressing is changed in 10 to 14 days unless there is a special indication for an earlier examination (Figs. 7–10). It was the author's privilege to see a number of cases reported by Farmer, and the results were far superior to anything he had seen in similar wounds treated by other methods.

There may be one refinement which could be added to Dr. Farmer's method. J. Staige Davis has shown that skin may be preserved for a reasonable period of time by refrigeration. Also, it has been stated that during refrigeration the differences between the portions of the skin that would normally

Fig. 10. The condition some months after accident. (Courtesy of Farmer, *Ann. Surg.*, 1939, 110: 952.)

live and the portions that are too severely injured to survive are demonstrated. Davis says:

"The idea is prevalent that skin grafts of all kinds must be applied either immediately or within a comparatively short time after cutting. Years ago the writer [Davis] became interested in the preservation of skin grafts, and has experimented with the refrigeration of various types. He soon became convinced that there was no hurry in applying skin grafts and that they could be preserved quite simply. If the grafts were to be used within 24 hours, wrapping them in sterilized dressings moistened with normal salt solution to keep them from drying and storing in the ice box were sufficient. If longer periods were required the grafts were stored in jars of sterile oil, vaseline or sterile albolene in the coil compartment of a mechanical refrigerator. The grafts when removed from vaseline or albolene are as pink as when they were put in, and look quite fresh. They are either wiped gently with sterile gauze to remove the vaseline or are washed with ether before being placed on the granulations. It was noted that while the refrigerated grafts would take and the blood supply become established it was fully a week, and sometimes longer, before any new growth of epithelium is observed from the skin margins and that this growth seemed slower than from immediate grafts of similar type. Microscopically no definite change was observed in the graft refrigerated, as above described, even after several months. Immediate autografts are always to be preferred, but refrigerated autografts have a distinct field of usefulness, and excess material can be preserved in suitable cases and used as required. Refrigerated small deep grafts are permanently successful and have been successfully transplanted after several weeks."

The usefulness of Davis' method in avulsion injuries can readily be seen, because there are

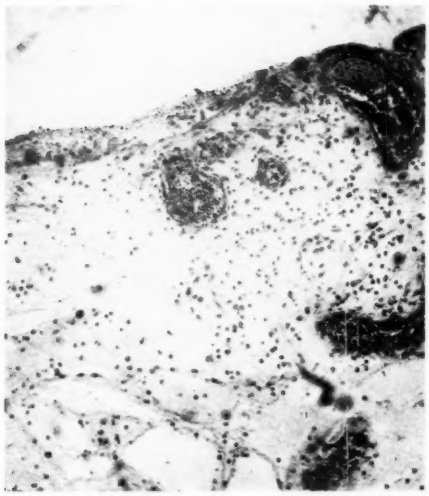


Fig. 11. High power photomicrograph showing edema of the superficial granulating area with slight degree of infection. Numerous blood vessels can be seen.

Fig. 12. High power photomicrograph of section at junction of granulation and scar tissue. *a* indicates the superficial granulation tissue; *b* the junction of the scar and granulation tissue; *c* the scar tissue.

some cases in which the muscle damage may be so great or the patient seen so late after injury that immediate skin grafting would be inadvisable. However, if one can preserve the uninjured skin and transplant it at a later time, a great saving can be made in hospital days and in suffering for the patient.

Avulsion injuries of the dorsum of the hand must be treated according to the depth of the injury. When tendons are exposed, immediate covering is essential. The insertion of the hand into an abdominal flap is advantageous when the injury is deep; when it is superficial, Farmer's method could be carried out by removing the avulsed skin and replacing it as he described. When the skin has been too severely traumatized, a full tissue graft taken from the thigh can be readily used. The replacement of the avulsed skin, even if split longitudinally as described many years ago by the Mayos, usually results in failure if any portion is left attached. Full tissue grafts may be readily utilized in similar injuries of the dorsum of the foot, provided the avulsed skin is not satisfactory.

In avulsed wounds that cannot be closed immediately and in which for any reason skin grafting is delayed for over 2 weeks, it is advisable to excise the underlying scar tissue rather than merely to remove the superficial granulations by curette. After several failures from delayed skin grafting following curettement of the superficial granulations, I dissected through the underlying scar tissue, which appeared red and healthy on the surface and was surprised to find rubbery firm avascular scar tissue extending often to a depth of 0.4 to 1 centimeter before healthy tissue appeared. Sections taken of this tissue reveal definitely the lack of vascular supply necessary to stimulate epithelization. The grafts appear healthy for a week or 10 days and then gradually melt away (Figs. 11 to 14).

Chemotherapy. In discussing the treatment of lacerated and avulsed wounds of the skin and soft tissues it has not seemed necessary to stress the use of sulfanilamide or similar preparations, either by oral or parenteral administration, because these drugs are being used throughout the country at large. Nor does it seem advisable at this time to recommend the local administration of these drugs at the site of injury. The experimental and

clinical results of local administration of sulfanilamide are as yet too uncertain either to advocate or condemn. When they have been used, it has been noted that there is an increase in the serous exudate, and this might be distinctly inadvisable if skin grafts are contemplated.

TENDON INJURIES

Tendons, like innocent bystanders, are subject to accidental injuries involving other structures. Extensive wounds of the skin and subcutaneous tissues frequently cause tendon damage as well. This is especially true of areas such as the dorsum of hands and feet, wrists and ankles, where the covering is thin and the bed unyielding. The most dangerous location for tendon injuries is in the flexor creases of the fingers and palm. This area is frequently traumatized by sharp cutting instruments and the tendons severed. If infection is not prevented, the extension of the pus along the tendon sheath will not only create slough of the tendons but may allow the infection to extend along the deeper spaces of the hand with irreparable injury. The possibility of tendon injury, therefore, must be borne in mind when apparently superficial wounds are treated; and repair of tendons, when injured, should be undertaken at the earliest possible moment consistent with good surgery.

The decision between primary and secondary suture of tendons calls for keen surgical judgment. In cases seen within 4 hours of injury primary suture may be done with reasonable expectation of an excellent result. This assurance is lacking, however, when dirt has been ground into the wound or the tendon extensively contused and devitalized. Primary suture is hazardous also if there is a question of contamination with human acclimatized bacteria or if antiseptics have previously been poured into the wound. In all such cases and in injuries more than 4 hours old, attention should be directed solely to cleansing and healing the wound, and the damaged tendon left for secondary suture at a later date.

When primary suture has been injudiciously performed and infection ensues, the patient is

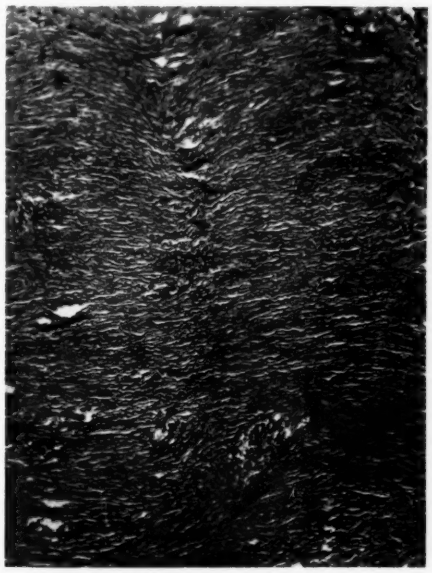


Fig. 13. Dense scar tissue in the region of the deeper area.

far worse off from the standpoint of eventual rehabilitation than if the tendon had been left for secondary suture because just so much tendon tissue will have been lost and scar tissue formed. Function is traded for deformity—a poor bargain.

Atraumatic handling of tissues, the avoidance of chemical antiseptics, and the use of fine silk sutures placed without tension are sound surgical principles worthy of particular emphasis in tendon repair. Tendon is a relatively avascular structure, its meager blood supply coming from a delicate sheath or from the surrounding soft tissues. At the time of repair, if the already damaged tissues are needlessly subjected to the additional trauma of rough handling and strong antiseptics or if the blood supply is impoverished by tense sutures, one must not be surprised should infection, with all its disastrous consequences, result.

Kanavel, Bunnell, Koch, Mason, and Loyal Davis have contributed largely to the knowledge of the physiology and histology of tendon repair and have presented for us definite clinical therapeutic measures based on sound

surgical principles. They have shown that connective tissue union takes place first between the apposed ends of a severed tendon. This process commences promptly after suture, is complete in 3 or 4 days, and is dependent upon restoration of continuity of the tendon sheath or surrounding soft tissues. In favorable cases tendon cells then grow across this connective tissue bridge and establish a complete tendinous union in from 10 to 14 days. The tendon at first shows distinct thickening at the site of repair and adherence to the surrounding structures, but in the course of a few weeks it becomes thinner, the adhesions are stretched, and freedom of motion is gradually established to a greater or lesser degree.

Bearing this in mind, one can appreciate the vital importance of an atraumatic technique in tendon repair, the use of fine, nonabsorbable, nonirritating sutures placed without tension, the elimination of exposed knots, and the accurate reposition of sheaths as well as tendons. Following repair, the parts should be splinted in the position of greatest tendon relaxation for a period of 2 to 3 weeks before active or passive motion is attempted. Physiotherapy, when initiated, must be under the direct supervision of the surgeon who, alone, is responsible for the end-result. Too often the importance of this period of rehabilitation is minimized, the after-care being placed in the hands of enthusiastic but inexperienced assistants. Such a practice cannot be too strongly condemned.

The principles discussed thus far apply to tendon repair in general. Secondary suture calls for special consideration. No attempt at secondary repair of tendons should be made in less than 3 to 4 weeks after injury in a wound which was closed and had healed *per primam*. If a mild wound inflammation or a mild staphylococcic infection was present, 6 to 8 months should be allowed to pass, and in the case of a severe infection or if a streptococcus was cultured it is safer to wait 12 to 18 months before a secondary tendon suture is undertaken. These time limits, are, of course, not absolute, but they serve as a fairly reliable guide to the condition of the tissues and the chances of relighting an infectious process.

Scar tissue in which the tendon ends have become embedded must be carefully but thoroughly removed by sharp dissection. Sometimes, when subcutaneous tissue is scanty and scar tissue excessive, a full thickness or pedicle graft must be transferred to fill the defect left by this dissection, in order to have sufficient subcutaneous fat surrounding the tendon to prevent re-formation of dense scar tissue adhesions. In this event actual tendon suture must be postponed until a later date.

The tendon ends must be completely freed of adhesions back as far as normal tendon sheath and any portion which cannot be freed will have to be excised. This excision may make it impossible to re-appose the ends of the tendon without tension. If this proves to be the case, tendon suture should not be attempted but a free tendon graft, complete with its sheath, must be obtained from another part of the body and used to fill the gap.

The exercise of sound judgment in the selection of cases for primary suture and courage to delay primary to secondary suture with a clear comprehension of basic surgical principles will, therefore, go far toward improving the results of treatment in acute tendon injuries.

SUMMARY

1. Hemorrhage and edema can cause extensive tissue necrosis in severely contused wounds. The early releasing of incisions may be necessary.

2. The criteria for and against primary suture in lacerated wounds and the technique to be followed are presented.

3. In order to prevent gangrene of the flap in avulsed wounds, an operation is described by which the skin is débrided and implanted as a full tissue graft in the defect. The possibility of preserving, by refrigeration, skin that cannot be immediately utilized is discussed.

4. The process of repair of sutured lacerated tendons is presented. The indications for and technique of primary and delayed suture are described.

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THE MANAGEMENT OF THE URINARY BLADDER IN TRAUMATIC LESIONS OF THE SPINAL CORD AND CAUDA EQUINA

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DISORDERS of bladder function which always accompany major spinal cord injuries are largely responsible for the high mortality associated with acute traumatic myelitis. This high mortality results from overflow incontinence with the development of decubital ulcers and urinary tract sepsis. Both of these complications can be minimized by proper management.

The rational management of the bladder in these circumstances depends upon a recognition of certain fundamental principles. Spinal shock which follows cord injury is always reflected in the urinary bladder by muscular atony, manifested clinically by urinary retention and overflow incontinence. The period of bladder atony is temporary, lasting from a few days to many months. Recovery of the bladder is manifested by alterations in its behavior, depending upon the extent and location of the cord injury. These alterations in behavior follow certain definite patterns, which may be recognized by appropriate examination.

There are three general types of recovery pattern. The first and most common of these is the reflex neurogenic bladder, produced by a transecting lesion above the conus (Fig. 1). In this situation, bladder activity is governed by a simple spinal reflex, synapsing in the sacral cord devoid of cerebral control. Filling of the bladder with resultant stretching of its wall constitutes the stimulus which results in bladder contraction and evacuation. This reflex evacuation is necessarily periodic, and, since it is anatomically dissociated from the higher centers, is not under voluntary nervous system control. The patient can neither initiate nor cause cessation of urination at will, but is periodically incontinent.

A second pattern of bladder behavior is seen following extensive injury of the conus or cauda equina (Fig. 2) with interruption of both the sensory and motor units of the reflex arc which controls the bladder. This externally denervated bladder has been properly termed the autonomous neurogenic bladder. Normal sensation is gone and voluntary or reflex micturition is abolished. Bladder muscle tone is increased, probably by its myenteric plexus. The internal sphincter is hypertonic. It is possible that this is maintained by the sympathetics via the (presacral) hypogastric nerves which are spared in cauda or conus lesions. The bladder always shows coarse trabeculation, an evidence of imbalance between sphincter and detrusor tone and carries a high residual. The intravesical pressure is high, and evacuation is by dribbling overflow since reflex activity is abolished.

The third, and last, type of neurogenic bladder results when only the sensory side of the spinal reflex arc is damaged (Fig. 3), which occurs in some partial destructive lesions of conus or cauda equina. This bladder behaves like the atonic bladder of tabes dorsalis, in which by an analogous mechanism the sensory unit of the arc has also been interrupted. Recovery from spinal shock is here followed by a persistent atonia of the bladder musculature. There is dribbling overflow incontinence from a bladder which has a low intravesical pressure and which possesses no reflex activity.

To summarize, following spinal cord injuries regardless of level, a period of shock with bladder atonia and retention occurs. Subsequently with recovery of neurological function, one of the behavior patterns in bladder function is manifested, depending

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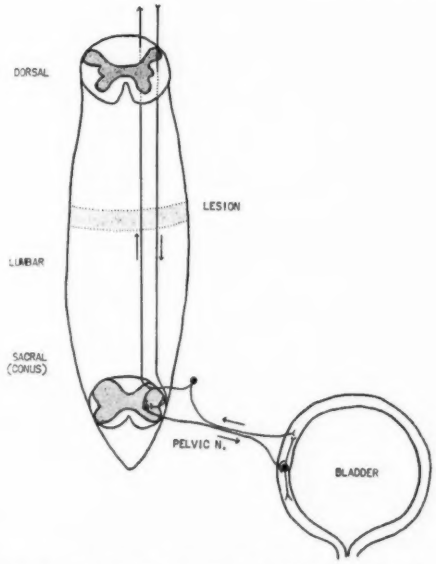

Fig. 1. The reflex neurogenic bladder is caused by a complete transecting cord lesion, above the conus. Bladder activity is controlled by a simple spinal reflex, synapsing in the conus. When the bladder fills to a certain capacity (100 to 250 c.cm.), the reflex is stimulated, causing bladder contraction. This bladder is characterized by periodic evacuations, without voluntary control.

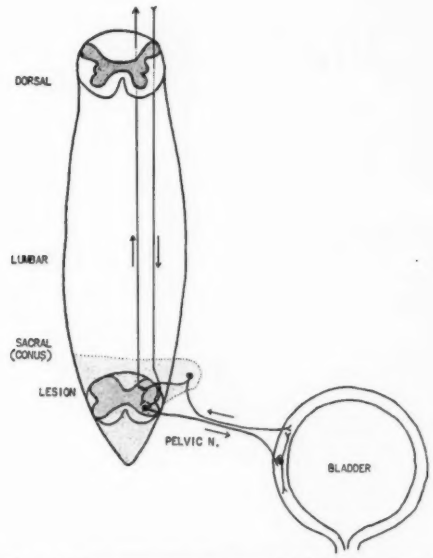

Fig. 2. The autonomous neurogenic bladder is caused by any lesion which destroys the conus or cauda equina. The bladder is completely deprived of external innervation, and depends entirely on its intrinsic myenteric plexus, whose fibers lie within the bladder wall. The bladder musculature and internal sphincter both are hypertonic. Despite the high intravesical pressure, the tonic sphincter acts as an obstruction. Since reflex activity is abolished, evacuation occurs only when the intravesical pressure exceeds the sphincteric obstruction. Voiding is by dribbling overflow. A high residual urine is present.

upon the extent and level of spinal injury. These are: first, the reflex bladder, when the lesion is situated above the conus, leaving the simple spinal reflex arc intact; second, the autonomous bladder, which has been completely denervated by extensive injury of conus or cauda equina; and, third, the atonic bladder, in which the injury has interrupted only the sensory side of the spinal reflex arc. If complete recovery from the nerve injury takes place, the bladder function ultimately becomes normal; otherwise these patterns are permanent.

The urological management of these cases concerns itself with two different periods: first, management of the bladder during the period of early atonia; and, second, the management of the chronic neurogenic bladder.

THE MANAGEMENT OF THE ACUTE NEUROGENIC BLADDER

The two cardinal dangers in management of the acute atonic neurogenic bladder are infection and overflow incontinence. Careful asepsis and proper drainage will minimize both of the dangers. Nursing care of these patients is greatly simplified by drainage of some type, and it has been demonstrated that the incidence of sepsis can be enormously reduced by properly managed drainage. Obviously, the circumstances under which the patient is encountered following injury will be an important factor in deciding the type of drainage employed and when it should be instituted. On the battlefield, the highway, or in the factory, aseptic urinary drainage is usually impossible; in these circumstances, overflow incontinence is more desirable than immediate catheterization. Since the entire management of traumatic myelitis is one which requires the facilities of hospitalization, urinary tract drainage should be deferred until this is accomplished.

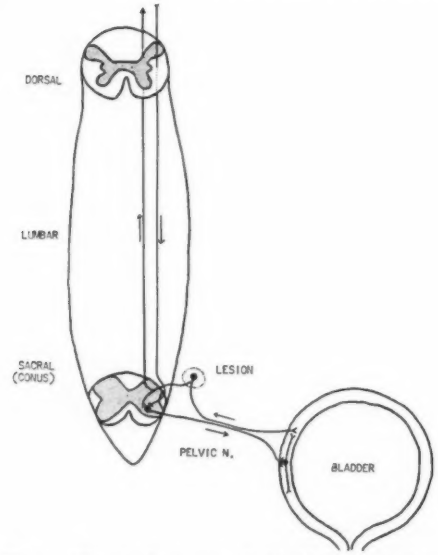

Fig. 3. The atonic neurogenic bladder is caused by a partial injury of conus or cauda equina in which the sensory pathways alone are damaged. Reflex activity is abolished by destruction of the sensory limb of the spinal reflex. Since sensation is lost the bladder is habitually overdistended until actual atrophy of its musculature results. The expulsive forces then become so weak that normal sphincteric resistance alone causes urinary retention. Voiding is by straining or dribbling overflow, with a constant high residual urine.

There are three methods of providing bladder drainage: intermittent catheterization, inlying catheter, and suprapubic cystotomy. Intermittent catheterization is undesirable because it does not provide continuous drainage and frequent catheterization increases the hazard of urethral trauma and fulminating infection. Continuous drainage, either by urethral or suprapubic catheter, provides the optimal condition for avoidance of sepsis and incontinence and for allowing the earliest return of bladder tone. The choice between these two methods of continuous drainage depends upon the hospital facilities available for providing the greatest degree of aseptic care of the drainage systems employed. Under ideal circumstances, urethral catheter drainage might appear preferable in that it avoids the necessity of a suprapubic wound. The inherent dangers of this method are to be found in the occasional severe genital infections which occur with inlying catheters in the male. It should be borne in mind that the inlying catheter drains the bladder but does not drain the urethra. Suprapubic drainage helps to avoid urethral infection and therefore this method is preferable under most circumstances.

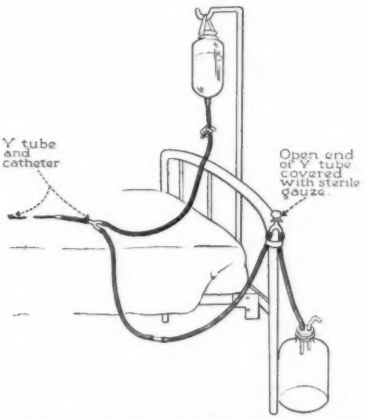

Fig. 4. The closed irrigater-drainage system. The entire system, wrapped in a sheet, is sterilized by autoclave. The reservoir bottle may be filled with any desired antiseptic solution. Periodic bladder irrigations are carried out by the nursing staff. Negative pressure drainage is maintained by closing the upper limb of the Y-tube. When positive pressure drainage is desired, the upper limb of the Y-tube is kept open and is covered with sterile gauze.

Continuous drainage by either method necessitates the maintenance of an aseptic drainage system if serious urinary infections are to be avoided. This may be provided by a sterile closed irrigater system, such as the one employed at the University Hospital (Fig. 4). Such a system enables periodic irrigation of the bladder with mild antiseptic solutions, thus controlling any existing infections, and is only disconnected or changed under aseptic technique, thus avoiding the introduction of new infection. Small doses of urinary antiseptics continuously given over long periods of time, when well tolerated, further aid in controlling infection.

Drainage is maintained until either complete bladder recovery or the final neurogenic pattern has been established. This transition into the chronic neurogenic pattern is recognized by cystometric examinations performed periodically.

THE MANAGEMENT OF THE CHRONIC NEUROGENIC BLADDER

1. The reflex neurogenic bladder which results from lesions above the conus is characterized by periodic incontinent evacuation. Its capacity of approximately 150 to 250 cubic centimeters allows satisfactory degree of comfort and continence in the patient whose intelligence allows him to adapt himself to its periodicity. Any factors which tend to increase the reflex irritability of this bladder reduce its capacity and increase the frequency of involuntary voiding. Infection and calculi are the common irritating factors and their prevention or elimination are of paramount importance in attaining the ideal status for this type of bladder. In our experience drug therapy designed to influence either the sympathetic or parasympathetic innervation of the bladder have had no clinical beneficial effect in this or any other type of neurogenic bladder.

2. The autonomous neurogenic bladder results from destruction of the conus or cauda equina, thus denervating the bladder. This bladder has no reflex activity; its intravesical pressure is high; the internal sphincter is hypertonic acting as an obstruction and the patient carries a high residual with overflow dribbling.

There are two methods of treatment. First, periodic manual suprapubic compression with straining in an effort to produce partial or complete evacuation of the bladder. When successful this method of evacuation provides reasonable relief of incontinence and is a satisfactory solution to the problem. Failure may result from too great an imbalance between the obstruction by the spastic internal sphincter and the forces available for evacuation. In this event transurethral resection of the internal sphincter may so relieve the vesical outlet obstruction as to allow satisfactory periodic evacuation as described above. We have resected a number of patients of this type with encouraging results.

Presacral neurectomy theoretically should relax the internal sphincter in these cases and facilitate manual evacuation of the bladder, attaining the same end as sphincterotomy. Our experience with sympathectomy in this group of patients is inadequate to warrant positive conclusions.

In the event that the above methods fail to result in satisfactory periodic evacuation with urinary continence, permanent suprapubic drainage or interval catheterization are required.

3. The atonic neurogenic bladder results from interruption of the sensory components of the reflex arc. This bladder is characterized by a low intravesical pressure, a relaxed internal sphincter and a high residual urine with dribbling incontinence. There is no reflex activity, so automaticity can never be hoped for. Periodic evacuation can generally be accomplished by manual suprapubic pressure with straining. In this situation, voiding is more easily accomplished than in the autonomous bladder in which a hypertonic internal sphincter exists. Permanent suprapubic drainage is rarely necessary since periodic manual evacuation is usually successful. Presacral neurectomy should be of no value in this type of bladder because the internal sphincter is relaxed.

The ideal to be attained in any patient having a chronic neurogenic bladder is periodic evacuation of the bladder with satisfactory urinary continence and the avoidance of urinary sepsis. This ideal can be attained even under the most trying circumstances with most patients affected with traumatic myelitis. Asepsis, antisepsis, an understanding of the physiological principles involved, and infinite patience are required in order to rehabilitate this group of unhappy individuals.

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THE PRINCIPLES OF SURGERY OF THE COLON

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IT is because today the language of surgery is a universal tongue that such occasions as this should signalize a generous expression of gratitude for the culmination of those works which have at the hand of many through the golden ages of time slowly found their way into the boundless coffers of our ever increasing wealth of surgical knowledge and experience.

It is a tribute to those of the four corners of the earth who have bent the shoulder of effort to the unhurried wheel of surgical progress in the tireless solitude of unheralded study. All this because no single surgical achievement, however simple, can stand alone, separated from the past, independent, and isolated from the future, for each tiny step in the common procedure of today has a background of generations of thought and experience.

Surgery, child of trauma, by necessity developed as a defensive and reparative act against the injuries of prehistoric man and animal. With the advance of civilization the demand upon the creative ingenuity of those who administer to wounds and trauma of war and industry has increased hugely.

Upon the fundamentals of traumatic surgery are based the entire field of the elective act as practiced today. Recorded first in the laborious hand of the scribes, and then in printed type are thousands of pages of history which preceded the heroic achievement of Ephriam McDowell, whereby abdominal surgery was born. Upon that memorable event whole new fields of surgical endeavor measureless to man were unfolded in a glorious panorama of the future, resplendent with the fruit of intellectual fertility, bursting with the vigor and enthusiasm of youth, though tempered by the judgment of ages and buttressed by centuries of industry, courage, and honesty.

In the field of surgery the thought not only of nations but even of civilizations has been woven together, oblivious of time, space, and belief, into a pattern which has created a universal brotherhood; a brotherhood with but one common interest, a tie far deeper than blood, far wider than race—the development and progress of surgery.

This progress has not been a steady, unimpeded rise based on the simple accumulation and correlation of scientific data, but like the cultural history of mankind it has often faltered—faltered because of the blind intolerance of ignorance shrouded in the cloak of superstition and nurtured by the charlatan and the mountebank.

Hampered again by the goading decimation of plagues or the devastation and destruction of warfare, it was still further retarded by the ravages of avarice, ambition, and envy; yet new milestones on the pathway of medicine continue to fade into the distance as have the footprints of the silent great who have left their everlasting mark in the pages of medical history.

In spite of turbulent periods of social conflict, economic uncertainty, and political unrest, the world of science alone is at peace. The true surgeon, a scientist at heart, though suffering the sorrows and pain of existing tragedy, may turn for consolation to the glories of scientific progress. Elective surgery, the last born progeny of the surgical art, records among its earliest efforts operations for benign and malignant lesions of the lower segment of the alimentary canal. Surgery of the colon proper, naturally, was held in abeyance until the Listerian era, which followed the discovery of anesthetic agents and permitted the deliberate invasion of closed body cavities without assuming inordinate risks.

It has progressed slowly step by step from the early elementary though ingenious attempts of Hippocrates to treat fissures, fistulas, and hemorrhoids, down to such extensive operations as segmental or total colectomy, the heroic one stage combined abdominoperineal resection of the rectum, and other quite formidable procedures commonly practiced

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today. Such operations are no longer euphoric dreams of the past, but a culmination of carefully correlated results of centuries of conscientious endeavor tempered with fortitude, persistence, and ingenuity.

The history of progress in this field of surgery has been punctuated with many of the great names in medicine, and to pause briefly in tribute to these sturdy pioneers is to avail ourselves of an opportunity perhaps too frequently overlooked in the turmoil of life's quickening tempo.

Hippocrates, Celsus, Paul of Aegina, John of Arderne and of the Arabs, such surgeons as Avicenna, Albucasis, and Rhazes, are foremost among the pillars of progress in the early treatment of rectal disease.

Morgagni, early in the eighteenth century, proposed the operative treatment of cancer of the rectum which was first attempted by Faget in 1739. However, Lisfranc is usually accredited with this achievement because of a thesis published by his pupil Pinault, who, in 1829, reported 9 cases in which Lisfranc used the perineal resection. Dieffenbach and Velpeau modified this primitive procedure, while Amussat, Verneuil, Kocher, and later Kraske, developed and popularized coccygectomy and the partial removal of the sacrum for more adequate exposure.

The development of surgery of the lower gastro-intestinal tract lagged behind surgery of the stomach and biliary passages for many years, perhaps without good reason, but it is a fact that the early pioneers of abdominal surgery made fewer attempts at correction of pathological lesions of the colon, instituted fewer research problems, and understood less clearly the physiology of this portion of the alimentary canal than of its fellow higher up. A few hardy souls persisted steadily and doggedly, however, to extend the surgical horizon with the result that today many lesions of the colon and rectum, hitherto ignored for one reason or another or deemed unapproachable by surgery, have found remedy or palliation by operative maneuver.

The development of colostomy, as a means of colonic decompression, was reported as used by veterinarians with success years before Praxagoras, in 400 B.C., opened the abdomen for ileus, incised the bowel to evacuate its contents, and then closed both bowel and abdominal wall. There is no available record of the outcome of this procedure, nor is there further mention of its use until 1710. At this time Littré is said to have performed a colostomy for imperforate anus in an infant, but not until 1776 was the procedure utilized by Pillore in the treatment of cancer of the rectum. Later DuBois and Duret performed colostomy for imperforate anus, but nearly a quarter of a century passed before left inguinal colostomy attained recognition in its present day usage.

Baudens, Keyworth, Ward, Allingham, and others continued in this field to develop modifications of the operation for posterior resection of the rectum, and, in 1880, Czerny, attempting such a procedure found the growth well up in the rectosigmoid and was forced to remove it transperitoneally. The operation was unintentional as well as unsuccessful, but the principle of the combined operation was discovered, although von Volkmann in 1889 is usually credited with having envisaged such a procedure which was later carried out by Miles with its recognized present day success.

In 1823, Reybard resected the sigmoid flexure for cancer in a man of 29, and made a primary anastomosis. The patient recovered but professional criticism served to discourage the popularity of so drastic a measure. Again, in 1843, Thiersch resected the colon for an acute obstruction, but by 1880, 37 years later, only 10 resections of the large bowel had been recorded, of which 3 were successful.

During the next 20 years, however, such names as Billroth, Marshall, Kraussold, Bloch, Mikulicz, Weir, and others are among those associated with the advancement of surgery of the colon, and to these persistent, bold, and enterprising masters, we, of the present generation of surgeons, owe a debt of homage for its modern status. Today the scope of application of the operative act to many lesions of the large bowel hitherto considered ill-fitted for surgery has been enormously broadened. Intractable ulcerative colitis, which has rendered the lower bowel a useless physiological organ or a distinctly harmful focus of infection, now responds favorably to total colectomy. Attack on megacolon through the sym-

pathetic nervous system brings about a normal bowel function in a high percentage of cases. Operations for complications of diverticulitis are routine in application and have definitely established indications and limitations. The surgery of adenomatosis coli is a favorable chapter and other pathological entities such as hyperplastic tuberculosis, fecal fistulas, benign tumors, intussusception, volvulus, etc., continually appear on the surgical list in all busy surgical clinics.

The most frequent and serious lesion of the colon and rectum which engages the surgeon's attention is cancer, and efforts to develop extensive, technical maneuvers for its radical extirpation and cure are continually being carefully thought out and scientifically tested.

Surgical extirpation of the growth is the only method of treatment which offers favorable prognosis. There is no other opportunity of cure, albeit certain agents of palliation deserve consideration. Nevertheless, prognosis following operation, which shows 61 per cent of cases without nodal involvement and 30 per cent of cases with nodal involvement free of cancer at the end of 5 years, certainly affords opportunity for optimism. In the lowest segment of the alimentary canal the outlook is even more favorable and the average percentage of cures from the clinics of the most experienced surgeons here and abroad shows 58 per cent of patients alive and well at the end of 5 years, including both those with and without glandular involvement.

When such figures are buttressed with the favorable mortality percentage of 6 to 10 per cent, and a resectability rate of approximately 75 per cent, the importance of increasing all known safety factors to insure favorable curability curves is emphasized, for the optimum of surgical treatment for any organic lesion demands a combination of these elements, and to this end offensive plans in dealing with lower intestinal malignancy have been triangularized into measures of co-operation between all professional groups concerned with both diagnostic and therapeutic measures. Safety factors of the greatest importance are: (1) relief of obstruction; (2) combatting dehydration, desiccation, and anemia by a period of pre-operative preparation; (3) local cleansing of the bowel during this period and the elimination of infection both by lavage and chemotherapy; (4) evaluation of the physiological reserve of the patient based upon laboratory procedures as well as physical examination and clinical appearance; (5) meticulous attention to operative detail and the adjuncts of time saving, gentleness in handling tissues, and particularly the choice and administration of anesthesia; (6) vigilant postoperative care under personal supervision.

The importance of rehabilitation from depletion which results from malignant disease often superimposed upon a local septic process demands careful scrutiny of the nutritional state of the individual and attempts to combat dehydration, lowered physiological reserve, and vitamin deficiency by the administration of blood, vitamins, and high caloric diets may not be overemphasized. Rehabilitation is second in importance only to decompression and exercises a direct influence upon an operative outcome both immediate and remote.

It is necessary to mention the use of an intraperitoneal vaccine as a method of increasing resistance to infection and its influence upon operating mortality. Formerly I felt convinced that a great drop in the mortality curve was the direct result of such a practice, but in recent years since its abandonment without detriment to mortality figures, the conclusion has been forced upon me that the method of intraperitoneal vaccination which I formerly employed was not a major factor of success. Convinced nevertheless that there is a potentially sound and logical basis for its use, it is my hope that continued experimental work along this line will eliminate the present dangers of its employment and crystallize the advantages accruing to its use.

The whole pattern of safety and progress reflected in the hospital casualty list and in morbidity and curability graphs indicates the huge advances from the technical standpoint which have made it possible to undertake radical surgery in this portion of the intestinal tract with justifiable enthusiasm. Boldness in attack on cancer here as elsewhere is essential to ultimate success, but planning must be to the end that the patient's elements of resistance are conserved to withstand radicalness

in execution. In consequence, while extreme methods useful to implement removal of malignancy are rewarded by low hospital death rates, it must be remembered that no radical procedure can be dissociated from a certain mortality secondary to remote complications. Increasing the safety factors has largely done away with immediate complications of operation, such as hemorrhage, leakage, obstruction, and other similar unfortunate sequelae, but the fact remains that in the majority of deaths following colonic operations, the lethal factor is peritonitis which is closely followed by pulmonary complications, such as embolism and bronchopneumonia.

This triad continues to harass abdominal surgeons, and although energetic, untiring efforts are continually being directed toward increasing peritoneal resistance, combatting circulatory changes, and pulmonary complications, there still remains a great risk both immediate and remote to any measure which involves removal of a segment of bowel.

In all efforts aimed at the extirpation of portions of the colon, experience, often bitter and disappointing, but always in the hands of surgical thinkers offering a suitable reward for its effort, has shown immeasurable progress in the last quarter century. It has come about that recognition of a number of essential steps among which decompression, rehabilitation, graded operations, and multiple types of operations are notable, has resulted in a huge reduction of mortality figures, an extension of the horizon of operability, and a roster of 3 and 5 years' freedom from malignancy which parallels the end-results of cancer therapy elsewhere in the gastro-intestinal tract, if it does not surpass it. These advantages have not been attained without the necessity of recording many failures before the principles which are now routinely acceptable were firmly established.

It is within the memory of even the younger surgeons of today that resections of the stomach, resections of the colon, ablation of the thyroid gland, sudden decompression of the urinary bladder, and prostatectomy were undertaken with little, if any attention, to preliminary preparatory decompression and restoration, in part or in whole, of physiological equilibrium. Aside from technical maneuvers which applied either in one or multiple stages have avoided many pitfalls of surgery inviting infection, the one principle of decompression perhaps has resulted in saving more lives than any single step in surgery for abdominal cancer. No longer is it justifiable; indeed, it is distinctly culpable to subject to a major procedure for a chronic ailment, an individual whose ability to resist surgical invasion has not been evaluated by careful estimates of the physiological functions of his several vital systems. In dealing with cancer of the colon the necessity of emptying the bowel of its content, of allowing time for the hypertrophied and dilated gut wall to return to normal and simultaneously to reduce infection around the local lesion is so obvious as to be beyond the stage of debate. Most cancers of the left colon and the rectosigmoid juncture produce some degree of obstruction at some time during their existence. Who has not had the experience of exploring an abdomen harboring a colonic cancer with complete confidence that the bowel was adequately emptied only to find on viewing the local growth, telangiectases prominent on the proximal gut, edema in the tissues of the mesentery, thickening of the entire bowel wall, a few enlarged glands adjacent to the growth, and other evidences of obstruction? The very nature of many growths, especially the encircling type so common in the left colon, predisposes to luminal stenosis. Further around in the right half of the large bowel, which is the physiological portion of the lower gastro-intestinal tract developed with and functioning as the small bowel does, one finds less tendency to obstruction but more often evidences of physiological imbalance. With local signs demanding decompression and rehabilitation, with laboratory evidences of failing cardiac capacity, a lowered renal function, and general physiological regression, one no longer questions the advantage of a preliminary period to combat physiological imbalance, to empty the lower gastro-intestinal tract, and to reduce local obstruction by adequate decompressive measures. Meticulous pre-operative measures are carried out as one phase of a surgical offensive supplemented by accurate, painstaking, and careful operative

maneuvers which in turn owe their selection to mature surgical judgment and are followed by a watchful postoperative care.

The immense advantage in operating upon many cancers of the colon and rectum by multiple procedures is recognized by all surgeons. It is probably a good plan for surgeons not particularly trained or interested in surgery of the lower gastro-intestinal tract to utilize graded operations more often than otherwise. Nevertheless, with increasing experience, better selection of cases, and more accurate preparatory programs, one finds the trend indubitably toward single maneuvers for cancer of the rectum, and in many instances for cancer of the colon as well.

The selection of operation and the choice of single or graded operation obviously is such an important safety factor that each case must be individualized, the gravity of the situation to each patient evaluated, and the operation fitted to the patient rather than the reverse.

The paramount issue in approaching an operation for resection of a segment of bowel is one of obstruction. As Tiffany quaintly remarked, "Resection in the face of obstruction is fatal," and increasing experience lends credence to his theme.

Modern surgery of the colon and rectum represents a sound practical attack on pathology based on a foundation of physiology which has been established by both experimental data and clinical observation. With the huge advance in pathological gradings, with the accuracy of diagnosis now routine in the hands of competent roentgenologists and proctologists, and with a large group of surgeons trained in the management of these cases, it is not strange that proper indication for operation and proper application of technical procedure to individual cases has broadened this field of surgery immeasurably.

In selecting a type of operation for removal of malignancy of the lower gastro-intestinal tract the principle of radical resection of not only the growth and the tissues immediately in juxtaposition but also the lymph-gland bearing tissues more distantly situated must be adhered to. In the colon itself the majority of its segments are supplied with blood through a relatively long, flexible, mobile mesentery which likewise houses the lymphatic system.

In the cecum, however, only about 20 per cent of the cases show a fully developed mesentery. The splenic flexure similarly is usually more or less fixed as is the portion below the rectosigmoid juncture. These areas, except for the splenic flexure, however, are richly supplied with lymphatics which are favorable to migration of malignant cells. These glands must be removed in any plan which is to be followed by a large number of long time survivals. The importance of removing gland bearing tissues distant from the original growth is recognized in dealing with cancer elsewhere and it is no less necessary to extirpate wide areas of mesentery in removing a colonic cancer than it is to do an extensive dissection of the axilla as a routine in operations for breast cancers or to apply the principles of dissection en bloc in orolabial malignancy.

The work of David and Gilchrist, published in 1938, and more recently supported by statistics from St. Mark's Hospital, London, demonstrates beyond peradventure the necessity of widespread tissue removal in cancer of the rectum. They showed that, in 68 per cent of resected rectal cancer specimens, glandular metastasis could be demonstrated by a painstaking examination of a large number of glands. What further proof is necessary to demonstrate the desirability of removal of a large portion of sigmoidal mesentery in dealing with rectal cancers?

It is futile to assert that it is impossible to do a gland dissection of the pelvis. Miles' beautiful demonstration of rectal lymphatics has established the fact that the majority of metastases take place in the upward zone of spread, namely, toward the sigmoid, and by his type of operation gland bearing tissues for rectosigmoidal and ampullary cancers are removed satisfactorily in the majority of cases.

In this connection it is permissible, I trust, to support the thesis that radical operations for removal of rectal cancers which carry out these established principles must furthermore include, as one of the technical details, the manufacture of an artificial stoma. This step necessitates the sacrifice of the splendid sphincteric mechanism of nature; a sacrifice which

the layman is always loathe to endure and one which many physicians are apparently reticent to recommend. It is true that any mutilating operation is a most unpleasant duty to perform, yet, in dealing with cancer, destructive and mutilating methods which may be proved statistically to save lives in a larger percentage of patients than less radical measures must be accepted.

The dislike of a colostomy is a state of mind which may readily be overcome by a sympathetic attitude to it, and in supplement a properly constructed stoma. Its possession entails no social ostracism and frequently but little interference with professional and social activities. The decision evidenced occasionally by surgeons to co-operate with the desire of the patient to save the sphincteric mechanism will be readily abated by a careful perusal of factual analyses, for operations which violate surgical principles are not followed by uniform success.

I would not be understood as condemning totally the employment of procedures for saving the rectal sphincters. I would even concede that in a low grade growth which has not metastasized, in many instances the operation may be useful. It would be interesting, however, and instructive to have criteria established which would permit us to tell without resection which cancers were still local and which ones had metastasized.

In removing segments of the colon, widespread resection of its mesentery is not difficult. The more important decision comes, first, between graded procedure or single stage procedure, and second, between immediate reestablishment of the gastro-intestinal continuity and delayed union.

Graded procedures, advantageous as they are, may be abandoned when an estimate of the patient's general ability to withstand a formidable intraperitoneal operation permits and the local conditions are satisfactory. Local conditions which influence the use of multiple maneuvers are: (1) fixation, (2) infection, (3) obstruction.

It is a well known fact definitely established by experimental and clinical research that the combination of obstruction and ulceration increases the permeability of the intestinal wall and permits the migration of organisms into the pericolonic tissues. Under condition of fixation the very act of mobilization encourages peritoneal contamination. However, in a sturdy risk in whom the growth is free and not firmly held to the lateral parietal peritoneum, and in whom the obstruction has been relieved by preliminary preparatory measures, one may, with confidence, employ a single stage maneuver of anastomosis and resection.

One may not easily overestimate the advantages of a complementary decompressive measure in the event one selects a single stage resection in either the right or the left segment of the colon. Whether one employs open anastomosis or aseptic anastomosis, the healing power is diminished in a cancer patient, particularly if the growth is in the right colon and is accompanied by the usual profound anemia without visible loss of blood. In consequence, about the third to the fifth day during the "lag-period" of healing, increased intraluminal pressure may compromise the suture line. This may be avoided by the use of a complementary ileostomy at the time of resection or the introduction of the Miller-Abbott tube after resection, as advocated by Whipple.

What method of suture is employed is largely a personal equation and arbitrary pronouncements, relative to the advantages of one type of suture or one type of anastomosis, are rarely fundamentally sound nor do they always reflect mature judgment.

As an advocate of aseptic anastomosis, I believe it is more desirable because it diminishes if it does not abolish the element of infection, and experience has shown that it may be accomplished with ease and satisfaction in the hands of most surgeons. At the same time it would be extremely dogmatic to urge that any single operative method to accomplish an objective so far outbalanced the disadvantages of all others as to make it indispensable. Elements of personality and circumstance must inevitably influence the choice of technique, and in consequence, the range of maneuvers continues wide and at the same time acceptable so long as fundamental principles are observed. The utilization of absorbable or non-absorbable materials likewise is more a matter of personal choice than of grave impor-

tance. The colon heals readily when it is approximated by suture to the small bowel for the blood supply of the latter is copious and plentiful. When joined segment to segment in its own continuity it likewise heals with relative kindness, for the blood supply of the colon, although less plentiful than that of the small bowel, is nevertheless of a constant pattern and adequate. The occasional leakage from efforts immediately to anastomose the colon is the result more often of infection at the suture line than it is of failure of the blood supply. True, failure of the blood supply secondary to infection and thrombosis accounts for a number of cases, but by and large vascularization to the cut ends of the bowel may be demonstrated by visual inspection.

For this reason it is comparatively easy to agree with those who advocate immediate anastomosis by suture in selected cases, always provided that a cecostomy has either preceded the resection or accompanies it as a complementary measure.

There are certain safety factors inherent to a delayed type of union which have proved not undesirable. Obstructive resection plus complementary cecostomy is an example of the operative act which accomplishes a radical removal of the growth and gland bearing segment of the mesentery without subjecting the patient to many of the hazards of immediate re-establishment of continuity by suture. The subsequent removal of the spur by pressure necrosis and healing of the wound completes a method which is accomplished with such a low mortality that it has appealed to me as a safe and satisfactory type of operation to be used in the majority of cases of cancer of the colon situated beyond the middle of the transverse colon.

It is difficult to agree with the opinion that the time element involved in this type of operation makes it less satisfactory than other procedures which carry a greater risk yet cut down the morbidity figures, for to integrate economic conditions with surgical judgment must surely lead to controversy.

In support of this thesis it may be pointed out that probably the greatest single technical factor in advancing colonic surgery was the discovery of the principle of exteriorization.

In the early nineties, it was found that a segment of bowel could be extraperitonealized, the abdominal wall closed snugly around it, and the removal of the tumor bearing loop postponed until nature had agglutinated wound surfaces and sealed off the peritoneal cavity. This discovery marked an epoch in colonic surgery by which mortality was hugely decreased and a great impetus given to a field of surgery hitherto granted frugal recognition by the medical world. Many names are associated with this type of operation, but it seems definitely established that Bloch, of Copenhagen, deserves credit for the first account of the principle published in 1891. In 1892, Recluse collaborating with Forgue published a description of 2 cases of exteriorization of the bowel without mentioning Bloch's name. Paul, of Liverpool, 9 years later, in 1900, published a modification of Bloch's method, ligating the mesocolon, abutting the two loops of bowel and decompressing the proximal loop by insertion of a glass tube. In 1902, Mikulicz, in the *Transactions of the Thirty-second Congress of German Surgeons*, spoke of the procedure which he alleged he had performed first in 1886. The operation so commonly referred to in this country as the Mikulicz operation, represents as is so often the case, the concepts of many surgeons, for discovery of a principle rarely comes as an isolated procedure, and more rarely as the work of one man. Multiple experiences, discussions, and researches combine to eliminate false impressions and establish truths in the birth of any principle, and so it is with exteriorization which is an ensemble of principles marking a new era in surgery of the large bowel. With its advent, danger of resection was largely reduced, leakage at the suture line was abolished, and utilization of the fact that nature's reparative processes by agglutination of approximated peritoneal surfaces were adequate, immediately popularized the method. As with all new methods there ensued a period in which its application, little understood, resulted in the customary abuse of a very new technique. Controversy early developed and still remains as to the desirability of ligating the blood supply in the mesentery of the bowel and bringing out a longer, more mobile loop. This step entails a certain

amount of danger, for necrosis and ulceration occasionally result in leakage into the peritoneal cavity, and death. Certain anatomical types make the bowel impossible of exteriorization, and a short mesentery filled with fat and inflammatory reaction becomes a distinct contra-indication.

With increasing experience at the hands of many surgeons both in this country and abroad, the definite limitations and indications of this procedure have been recognized and its place in the armamentarium of the modern operator firmly established. With the impetus given to surgery of the colon by the reduced mortality accompanying exteriorization, many other procedures were evolved for extirpation of cancers of the right and left halves of the colon in single, double, and even triple stages.

The ultimate aim of all types of operation for cancer is cure, but it must be recognized that there is a definite group of cases in which cure being impossible, the ingenuity and resourcefulness of the surgeon may still be available in the application of palliative procedures. Such a decision, often difficult in the extreme, is a function which no surgeon may escape, for trying as it is, it demands a not inconsiderable amount of courage as well as superb surgical judgment. One must often decide whether resection as a palliative measure is justifiable or whether because obstruction is not present the abdomen is closed and the individual permitted to languish agonizingly from multiple metastases and the ultimate lethal sequelae of carcinoma. It is a not uncommon experience to explore a patient with a cancer of the colon which is freely movable, and resectable with a reasonable mortality risk, and to find by palpation of the liver surfaces multiple umbilicated, irregular, malignant nodules. Removal of the local growth, precluding obstruction, fixation to neurogenic elements, and other painful complications, is often warranted under such circumstances, even though the mortality figures may be higher than in more hopeful cases. Death from cancer of the liver is a not too painful experience and in such circumstances, removal of the primary growth and consequent comfortable prolongation of life, is entirely praiseworthy. When obstruction has supervened with fixation, abscess formation, or other local complications with or without metastasis, drainage procedures either by bringing the alvine discharges to the outside through colostomy, or by-passing them by entero-anastomosis, give comfort and relief from the distressing period of impending dissolution.

The realm of palliative surgery has been somewhat overshadowed by the emphasis placed upon curative procedures, but in the treatment of neoplastic disease one cannot submerge the humanitarian interest in order to effect a surgical masterpiece of technical perfection, while the sufferer is offered no relief because he fails to comply with the rigid postulates of the curative endeavor.

The progress of scientific endeavor has during the last century done more to relieve suffering, to improve health, and to prolong life, than has been done during the entire span of civilization up to this time. It is because of this ever accumulating wealth of knowledge that the effort of intensive concentration has been father to specialization. In consequence, surgery of the colon and rectum has proved worthy of high rank in the surgical domain, for accomplishment has reached heights far beyond the fondest expectation of those tireless workers who laid the corner stone in the temple of our guild.

If, however, further discoveries in biochemistry and allied sciences displace surgery in the treatment of cancer, and as Dabney puts it, "cancer is ever shown to be a systemic disease, the technical literature on the radical removal of malignant lesions may become as obsolete as that of pouring burning oil into wounds," still the record of these operative maneuvers will remain as a monument to the persistent effort, skill, and ingenuity of surgeons of the past and present generation, and their vast achievements will continue to live in the glorious realm of tradition.

Complex problems both of physiology and pathology and changing trends in treatment testify that surgery in this field has not reached its ultimate, despite the well known tendency of great surgeons, consummating a meritorious career to deplore the fact that "there are no new worlds to conquer." From Paré, Vel-

peau, Moynihan, and other masters, such laments have come, yet strangely enough after each declaration some new discovery in surgery has been announced. Surgery of the colon is no exception and new advances in this field, limitless in opportunity, will continue to crown the endeavors of those who strive zealously and with the energy, ambition, and intelligence characteristic of the progressive minds who have planted markers of surgical discovery and who have written chapters in medical history.

HEPARIN IN THROMBOSIS AND BLOOD VESSEL SURGERY

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THE experimental proof that heparin would prevent thrombosis opened a field for a progressive advance in the surgery of diseases and obstruction of blood vessels. The important discovery of heparin by Jay McLean in Howell's laboratory was the first step in providing a substance which would prevent thrombosis and allow of certain operations which otherwise were doomed to failure because of recurring thrombosis at the site of operation. The final purification of the substance by Best, and Charles and Scott thereby provided a substance which was nontoxic, and placed it on a footing so that it could be used clinically.

The proof of the effectiveness of heparin to prevent thrombosis was obtained when it was shown that heparin would prevent experimental thrombosis in veins (4), thrombosis at the site of arterial anastomosis, and also thrombosis in venous grafts in an arterial tree. It was shown also that it would prevent recurring thrombosis at the site from which an experimental embolus had been removed and its effect in preventing thrombosis in the portal system was also demonstrated.

These experimental facts demonstrated the possibility of this substance being used in clinical cases in which repair of injured important arterial and venous trunks would be an advantage, extensive venous or arterial thrombosis was occurring, embolic occlusion of main peripheral arteries had occurred, or in which thrombosis of portal vessels was a factor, such as following splenectomy or following resection for mesentery thrombosis. Its use in diseases in which there is extensive thrombosis, such as in osteomyelitis and coronary artery thrombosis, has not been thoroughly investigated but warrants some investigation.

With a purified nontoxic preparation of heparin available, my associates (3) and I began administering it to clinical patients. It had been given clinically to prevent clotting in blood transfusions by Mason and McClure (2) but it produced toxic effects and did not come widely into use clinically. To date about 700 of our patients have been treated with heparin in sufficient doses to raise the clotting time to two or three times the normal level. Except for a few months in 1939 when there were definite thermal reactions in about 50 per cent of the patients receiving it there have been no toxic effects. The patients experience no sensations whatever as a result of the heparin administration, no more than the effect of an ordinary intravenous saline. The chief disadvantage of treatment with heparin is that it is necessary for the patient to be in bed to receive the continuous intravenous injection. The effect of heparin is so evanescent (the clotting time of a patient will return from 15 minutes to normal within an hour after the injection has stopped) that it must be administered continuously. Unfortunately, intermittent injections two or three times a day are impracticable because to make the effect of heparin last a few hours, so much must be given that the clotting time is elevated to several hours which, of course, is undesirable and might be dangerous.

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There are no contra-indications to giving heparin except in the case of a patient who has active bleeding from an open vessel, when the prolonged clotting time will encourage the bleeding to continue. The indications for heparin are in conditions in which it is desirable to prevent thrombosis in vessels or to prevent extension of an already existing thrombus. This, of course, applies to many medical diseases and to many patients following operations. Its administration is specifically indicated if the operation has involved a direct attack on blood vessels, such as opening a lumen, or under conditions in which suture, repair, or grafting of a blood vessel is necessary.

Heparin has been used with satisfactory results in the cases presented herewith. While many of these operations might be undertaken and results might be successful without the use of heparin, still with its use, success is insured and the results have been most satisfactory.

ARTERIAL SUTURE

End-to-end suture of arteries has been done successfully in several cases and the circulation and pulsation have been maintained in the periphery. Three only of these cases will be cited.

CASE 1. A man, aged 60 years, while using a hammer, had a piece of steel enter the upper arm about 2½ inches above the elbow. Immediately there was violent hemorrhage. When this was controlled a large swelling developed in the arm and this was accompanied by severe pain over the distribution of the median nerve. Clinical examination within 3 weeks demonstrated a mass with expansile pulsation and with a bruit over it. It was obvious that this was an aneurism of the brachial artery with pressure on the median nerve. The circulation to the extremity was normal although the pulsation in the radial and ulnar arteries at the wrist was very feeble. The median nerve pain was so severe that the patient asked to have his arm amputated and for this reason it was decided to operate upon this swelling at an early stage. The brachial artery was found divided about half way across. This opening communicated with a false aneurism about 2 inches in diameter. The aneurism was removed. The rent in the artery was of such a size and shape and with thickened friable margins that it was unsuitable for suture. Therefore, it was decided to divide the artery across and trim off the ends. By moderate flexion of the elbow, the divided ends were easily brought into apposition when an end-to-end anastomosis with a continuous fine silk suture was carried out without difficulty. Heparin was injected to fill the vessel at the site of the anastomosis. Immediately following the restoration of circulation normal pulsation returned in the vessels of the wrist. A continuous intravenous injection of heparin was given for the next 3 days keeping the patient's clotting time at about 15 minutes. The circulation remained normal in the extremity. The median nerve pain disappeared and the patient returned to his work as a laborer 4 weeks after the operation.

CASE 2. This patient, as the result of a motor car accident, had the brachial artery torn completely across about 1½ inches above its bifurcation. The patient, was seen several hours following the accident. The arm was greatly swollen, and with its change in color, loss of sensation and motion, with loss of pulsation at the wrist and loss of heat, it obviously was in a pregangrenous condition. At operation the ends of the artery were found separated by about 1½ inches and both ends were plugged with blood clot. The clots were removed. The ends of the vessels were trimmed and with a continuous silk suture a satisfactory end-to-end anastomosis was carried out. The patient returned to his work as a garage mechanic 6 weeks following his operation. He has been able to continue at his work for more than 2 years with a hand which is normal in all respects.

CASE 3. During a neck operation an excellent surgeon had the misfortune to damage a common carotid artery dividing it across completely. About ¾ inch of the length of the artery was resected to remove the damaged portion of the vessel. By flexion and lateral bending of the neck the ends were brought into apposition and a satisfactory end-to-end anastomosis was completed. This restored the circulation as indicated by a normal pulsation distal to the site of the anastomosis. Heparin was injected continuously over the next 8 days. The circulation was maintained through the artery and the patient had no ill effects in the way of cerebral symptoms, either from anemia or embolism, as might be expected to occur in up to 25 per cent of such cases had the artery been ligatured.

ARTERIOVENOUS FISTULA

While arteriovenous fistula may be treated surgically in a variety of ways, it is now possible with the use of heparin to resect and repair the vessels satisfactorily if this seems desirable. This has been carried out on several occasions.

CASE 1. A bullet wound in Scarpa's triangle had produced two arteriovenous aneurisms between the superficial and deep femoral arteries and their corresponding veins. The damaged segments of the vessels with the aneurismal sacs were removed and the vessel reconstructed satisfactorily and heparin administered intravenously. The circulation and

pulsation in the extremity has remained normal since that time, now 1½ years since the operation.

Two other such fistulas of blood vessels have been removed and the vessels repaired, thus restoring normal circulation to the extremities.

VENOUS GRAFTS

When segments of major arterial trunks have been destroyed by accident or pathological lesions, the usual procedure is to tie the vessels involved. Attempts have been made to bridge gaps in important vessels, but from the cases recorded the results have not been satisfactory because of thrombosis causing occlusion of the involved area. At many points large vessels may be tied without danger but in such vessels as the internal carotid, major vessels of the extremities, and the aorta, disaster is apt to follow their ligation. It was with great satisfaction, therefore, that aided by the use of heparin we have been able to place venous grafts to bridge gaps in important arteries on 4 occasions. In 3 of these the circulation was restored and maintained perfectly. In the fourth, because of gas gangrene in the extremity resulting from the accident, amputation was required.

CASE 1. A popliteal aneurism, rapidly enlarging and about to burst through the skin, caused the patient to have severe pain. It was obvious that some relief was needed urgently, so at operation the aneurism was resected. This left a gap of 3¼ inches in the popliteal artery. The remaining segments of the artery were greatly dilated and the walls were thickened and calcareous. While ligature of both ends of the vessel might have given a satisfactory result, the danger of gangrene from ligation of the popliteal artery was also considered. It seemed that this was a suitable case in which to attempt to apply a venous graft. The external jugular vein was removed and the gap of 3¼ inches was satisfactorily bridged by a double end-to-end suture of the graft to the segments of the artery. There was considerable difficulty in matching the small size of the vein to the larger size of the artery. This caused considerable stretching, especially where the greatly dilated proximal segment of the artery necessitated great stretching of the vein to complete the anastomosis. Following the injection of heparin, the circulation was restored with normal pulsation appearing in the vessels of the foot. The circulation remained normal in the foot for 2½ weeks. At this time there was a sudden recurrence of pain in the popliteal space. On examination there was pulsation of a mass and a bruit which could be heard with a stethoscope. It was obvious that another aneurism had formed. The area was again explored. It was found that the circulation was still being carried on through the graft. Its wall was thicker and the lumen was greater than when it was applied 2½ weeks previously. These changes corresponded to those which were demonstrated in the experimental venous grafts. Just distal to the proximal suture line, the anterior wall of the venous graft, where it was unsupported by living tissue and was running across a large cavity in the popliteal space, had given way and a small false aneurism had formed. On exploring through this opening it was demonstrated with a probe that the lumen of the graft was patent and that there was no stenosis at the suture lines. In spite of the urge to recover the specimen, it was decided to repair the aneurism of the venous graft. Flaps were cut in such a fashion that the lumen of the vessel was maintained and the aneurism was repaired. More heparin was injected and following restoration of the circulation there was excellent pulsation in the graft and the distal segments of the artery. The circulation has remained normal for more than 2 years, and the patient has been able to return to his work.

This was a most instructive case as it demonstrated the possibility of using a venous graft in an artery in a human being. It showed that when the patient is treated with heparin the graft survives; it does not become occluded or stenosed; its lumen increases in diameter; and its wall becomes thickened and such a graft can maintain a circulation in a major arterial branch for a period of at least 2 years.

CASE 2. A young man had the misfortune to divide the femoral artery with a pen knife. By prompt surgical intervention by an excellent surgeon who tied off the vessel, the violent hemorrhage was stopped, and with transfusions the patient survived. Within 12 hours there was some doubt if the extremity would survive. At this time he was operated upon by me. When the damaged ends of the divided femoral artery and vein were removed, there was a gap of 2½ inches in the artery and a smaller one in the vein. It was impossible to bring the ends into apposition by any position of the knee or hip. For that reason a segment of the adjacent vein which was already tied off was removed. The vein was turned inside out and the valve cusps removed. With this 3 inch piece of vein the gap in the artery was bridged successfully and heparin was injected. When the circulation was restored, excellent pulsation appeared in the vessels at the foot. Heparin was injected continuously for the next 8 days and then stopped. The pulsation of the vessels at the ankle was recorded every hour during this time. It did not decrease or change throughout this

time and has persisted, and the circulation of the extremity has been normal since the operation 4 months ago. The patient began walking about in 3 weeks and has been quite active since that time. There has been no aneurysmal dilatation of the graft and normal pulsation can be felt quite readily in the upper part of Scarpa's triangle. There is a slight bruit over the graft but this is not changing. There is no atrophy of the extremity and sensation and motor power are normal.

CASE 3. A patient, aged 72 years, had a direct injury over the base of Scarpa's triangle. Immediately following this a large hematoma developed in Scarpa's triangle which extended through beneath Poupart's ligament into the iliac fossa. This was obviously a false aneurism. The lump was enlarging rapidly and it was obvious that it was about to burst through the skin. It was operated upon, and the common femoral artery just below Poupart's ligament was found fractured across. The ends were thick, calcareous, and extremely brittle; these were trimmed back until fairly normal vessel wall was obtained. This left a gap of 4½ inches. The adjacent femoral vein was completely occluded by thrombus, the extremities of which could not be reached through the incision. A segment of this vein 4½ inches in length was removed. The thrombus in its lumen was very adherent to the wall so that it was necessary to turn the vein inside out and scrape the intima to clear it of thrombus. The cusps of a valve were clipped off so the thrombus could be removed from beneath them. This left a roughened, shaggy intimal surface. The vein was turned right side out again and with a double end-to-end suture the gap in the artery was bridged. Heparin was injected and the clotting time of the patient was kept at a level of about 15 minutes. The circulation and pulsation in the vessels of the foot were normal. Within a few days the patient died of a cerebral vascular accident, and the specimen was recovered from the thigh. This showed healing of the suture lines with healing of the roughened intima of the venous graft so that it was smooth and shining. There was no clot or thrombus at any point in the venous graft, at the suture lines, or in the adjacent segments of the artery.

This was a very severe test of the effectiveness of heparin in preventing thrombosis. From the exceilent result, with healing and return to normal of the wall of the venous graft, more evidence is provided that a clotting time of 15 minutes produced by heparin is quite adequate under the most unfavorable conditions.

EMBOLECTOMY

This operation has been questioned in recent years by physicians and surgeons alike, because of the high incidence of thrombosis at the operative site, following the removal of an embolus. This is much more apt to happen if the operation is undertaken more than 10 or 12 hours following the occurrence of the embolism. With the use of heparin, however, the picture has been entirely changed. With the use of this substance, the operation may be undertaken successfully up to 24 hours following the accident and if the vascular tree has been completely cleared of obstructing clot and thrombus and with the proper administration of heparin, the wall of the vessel will heal without further thrombosis and the circulation and pulsation in the extremity can be maintained.

Seventeen arterial embolectomies have been done and heparin used postoperatively. In this group the circulation was completely cleared of obstruction and the circulation and pulsation at the extremities remained normal in all.

In 2 of these patients the bifurcation of the aorta was completely obstructed by a massive embolus. This was removed successfully in both cases, the circulation and pulsation was restored successfully, and both patients made excellent recoveries from the operations.

With embolisms occurring in the vessels of the extremities, the operation is a relatively minor one and can be done quite successfully under local anesthesia. With the administration of heparin, the certainty of good results is insured. It is advocated, therefore, that the embolus be removed early and the patient be treated with heparin, rather than that the patient be allowed to continue to suffer and at the same time to face the dangers and disabilities of impaired circulation in most cases, and gangrene in some.

MESENTERIC THROMBOSIS

Every operating surgeon is aware of the extremely high mortality in cases developing mesenteric thrombosis. With the use of heparin if started at or immediately following the operation, the prospects of recovery are very greatly improved. Six patients of this type, in all of whom resection of intestine was necessary, were treated with heparin following operation. Four of these survived and are still alive and well, now more than 2 years after their operations. Two of the patients died of

other lesions but in neither of these was there extension of thrombosis in the portal system, which is the usual course following operation for this disease.

THROMBOPHLEBITIS, PHLEBOTHROMBOSIS, AND PULMONARY EMBOLISM

The prolonged morbidity with the discomfort and permanent disability following this disease lead one to try using heparin in these cases. It has been interesting to see the results of treatment in more than 125 patients. During the early acute phase of the disease the pain and aching is improved within a few hours and usually has mostly disappeared between 24 and 48 hours. The temperature, swelling, and tenderness also show improvement within the same period. In this group of cases the patients were treated for periods varying between 4 and 8 days at which time the patients were going about actively and were discharged from hospital. While it is difficult to arrive at the truth, one is impressed that there is less residual edema of the legs when the patient has been treated with heparin than in corresponding cases in which patients have been treated by other methods.

When pulmonary embolism has occurred and the patient has survived long enough to have heparin administered intravenously, there has been striking clinical improvement. While there is no reason that further embolisms should not occur in these patients, as heparin will not dissolve or remove clots or thrombi, still in 46 cases of this nature this accident has not occurred, except possibly in 2 patients who might have had further small embolisms. However, this was not proved, and the patients recovered. The 44 other patients had no further attacks of embolism and showed rapid clinical improvement.

This experimental and clinical work was carried out in collaboration with Professor C. H. Best. Miss Chute, Mr. L. Jaques, Dr. R. Wilkinson, Dr. P. Perrett, Dr. Ross MacKenzie, and Dr. J. Janes assisted during various stages of this work. Assistance from The Banting Research Foundation, Connaught Laboratories, and Mr. J. S. McLean in providing finances and material to help carry on this work is gratefully acknowledged.

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SYMPOSIUM ON CANCER

THE PRESENT STATUS OF CARCINOGENS AND HORMONES IN CANCER RESEARCH

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IN a previous communication the status of our knowledge concerning the etiology of cancer was reviewed (93). The rôle of the inciting carcinogenic factors including the hormones was presented from the experimental and clinical evidence as of that date. Since that time, there has been a marked increase in the number of investigations directed at these problems, now partly interrupted by the advent of the second World War.

It was but natural that the first enthusiasm of the research worker was to produce cancer in many forms and in many species with the new tools which served as inciting agents. The purified chemicals offered an easy weapon to produce carcinoma at will. The chemists industriously turned out new chemical combinations, changing their organic compounds by almost magic manipulations. The biologists then tested these agents for their cancer inciting qualities. It soon became evident that this type of research could proceed indefinitely. The emphasis accordingly shifted to the mechanism by which these carcinogenic agents brought about the process which is cancer.

In this paper, the more recent developments in the field of the carcinogenic agents, including the hormones, will be reviewed. Emphasis will be placed especially on the chemical carcinogens, light effects, and the hormones. The viruses will be considered only when they offer some fact bearing on the general problems. They constitute an important but complicated study in their own right.

Excellent reviews on chemical compounds as carcinogenic agents have been written by Cook and Kennaway (23, 24), Cook (22), and Fieser (41).

The most important cancer producing constituent of coal tar is 3:4 benzpyrene. It is insoluble in water or aqueous salt solution, but is soluble in the serum of animals, especially fat fed ones. It probably enters the cell by dissolving in the cell lipoids. It is found only in the higher fractions of coal tar because of its high boiling point. Convincing evidence that this hydrocarbon is concerned in the etiology of human cancer has not been produced. The possibility of lung cancer arising from some such agent in motor exhaust fumes, road tar dust, etc., has been investigated without definite proof of such an origin.

Methylcholanthrene can be obtained from cholic acid, the chief acid of human bile (Fieser and Newman, 42). For this reason it seemed more likely as a possible etiological agent in human cancer. It has been shown to have a very considerable potency as an inducer of malignant tumors in rats and mice.

It is true that 1:2:5:6 dibenzanthracene is more soluble in serum than 3:4 benzpyrene. It has been less effective as a carcinogenic agent in rats and mice than the two other aforementioned chemicals. The average time for the induction of tumors has been considerably longer as well.

The three carcinogenic chemicals named have been used in various vehicles such as lard, olive oil, paraffin, cholesterol, benzene, or alcohol. They are insoluble or but sparingly soluble in most of these reagents. Colloidal solutions also have been employed. Often the crystals of the carcinogenic hydrocarbons may be found in the subcutaneous tissues at the end of the experiment. The difficulty of distinguishing a tumor growth from the vehicle carrying the carcinogen has been considerable at times.

Both carcinomas and sarcomas have been induced by all three of these carcinogens in rats and mice by epithelial painting and by subcutaneous injection. In general, sarcomas in mice have been brought out more quickly than epitheliomas. Sarcomas in rats have been induced in about the same time as epithelial tumors in mice. The latent period between the application of the chemical and the appearance of the tumor has varied with the strain, the sex, the vehicle, the dosage of chemical, and the tissue involved. Apparently

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these carcinogenic hydrocarbons have been able to induce squamous cell carcinomas from any epithelium possessing such latent potentialities. In addition to the usual cancers of the skin and spindle cell sarcomas of the subcutaneous tissues, squamous cell carcinomas and sarcomas of the prostate have been induced in rats by benzpyrene (91), hypophyseal tumors in rats by the same agent (106), squamous cell cancers of the stomach in mice fed benzpyrene by mouth (45, 81, 144), osteosarcoma in a mouse by benzpyrene (13), tumors of the lung (131) from intratracheal injections of methylcholanthrene or 1:2:5:6 dibenzanthracene, tumors in the esophagus and peritracheal tissues from methylcholanthrene (140), tumors of the brains of rats (145) and mice (128). Nicod and Regamey called attention to the exaggerated sensibility of the connective tissue to methylcholanthrene and benzpyrene. They were unable to produce tumors of the parenchyma of organs which were injected with these substances because of the fact that the connective tissues gave sarcomas first in each instance.

In mice of known genetic constitution, C 57 brown, Mider and Morton (88) noted the remarkable fact that occasionally benign and malignant epitheliomas followed a single painting with methylcholanthrene. The usual sequence for such events has been a long continued repeated application of the carcinogen. The same investigators (89, 90) have been able to show a marked reduction in the latent period for spontaneous lymphomatosis and spontaneous mammary carcinomas in the dilute brown mice of Little, when they were painted repeatedly with methylcholanthrene. Apparently these carcinogens can bring out the latent potentialities of the tissues of the tested animals for tumor formation. Hence, the importance of knowing the biology of the strain under investigation for a proper interpretation of the carcinogenic properties of the chemical.

The smallest dose of 1:2:5:6 dibenzanthracene known to induce tumors has been determined by Dobrovolskaïa-Zavadskaïa (33). Single doses of 0.01 milligram, 0.005 milligram, and 0.0025 milligram were injected subcutaneously. Tumors appeared with the first two groups but not with the third.

By using different dosages of methylcholanthrene in different methods of application, Mahoney and Morton have been able to bring out several different tumor types (lymphomas, cancers of breast, lung tumors) in mice of the dilute brown strain, subline 212.

Cottini and Mazzone tested the effect of repeated applications of 3:4 benzpyrene to the human skin. Daily applications of a 1 per cent solution in benzol for periods not exceeding 4 months resulted in definite manifestations localized to the treated areas. Erythema, pigmentation, desquamation, the formation of verrucæ, and infiltration developed in chronological order. Upon suspension of the applications there was complete regression of the lesions within 2 or 3 months. These changes are believed to have been the early stages of a process which would have gone on to neoplastic proliferation ultimately had the applications been continued. The alterations were more pronounced in the older than in the younger individuals; and more so upon the unprotected skin surfaces.

Cook and the Kennaways (25) succeeded in producing an epithelioma in a mouse after application of deoxycholeic acid, a normal constituent of the bile. It took 776 days and occurred in only 1 of 80 mice painted. But subcutaneous injection caused the appearance of 3 spindle cell sarcomas in 5 mice which lived over 6 months. This confirmed the report of Ghiron. He found that deoxycholeic acid induced fibrosarcomas in a high proportion of rats and mice injected. The tumors were transplantable. The importance of these observations cannot be overstressed, as they indicate the possibility of malignant tumor production from a compound normally present in the human body.

Numerous substitution products of these three well known carcinogenic hydrocarbons have been synthesized and tested. The importance of the position in the ring, of oxygenation (26), of the methyl derivatives (130), of hydroxyl groups (23), of diazo coupling (41), etc., have been considered. These studies have been of great interest to the chemists. The London group determined that increasing the length of the carbon chain produced a rather irregular diminution of carcinogenic activity. The limit of activity seemed to be reached when seven carbon atoms were in the chain. None of these new compounds have exceeded the carcinogenic activity of methylcholanthrene.

In addition to the three carcinogens just discussed, great interest has been aroused by the production of visceral tumors in rats and mice. Kinosita added a 3 per cent solution of dimethylaminoazobenzene (butter yellow) in olive oil to the diet of rats for 50 days. Cancers of the liver were induced. These tumors metastasized. They could be transplanted. Cancer also was brought about in the livers of mice but not in rabbits or chickens. Rats developed liver cancers in re-

sponse to subcutaneous injections of this compound. Direct application to the viscus in cholesterol pellets failed in producing carcinomas.

Some other chemicals of naphthalene and carbazole groups have been found to produce liver tumors recently (22). Nakahara et al. (101) found that liver feedings inhibited the development of liver cancers in albino rats subjected to Kinosita's experiment with butter yellow. The same investigators (102) found also a slight inhibiting effect from yeast though the rats developed cirrhosis. However, crystalline vitamin B_1, failed completely as an inhibitor.

The mystery of carcinomas of the gastro-intestinal tract seemed to be on the way to solution when Roffo (121) announced that he had found such growths to follow the ingestion of fats oxidized by heat. He noted erosions, ulcers, and neoplasms of the stomach, liver, and cecum in rats fed on bread and milk to which there were daily additions of animal fats or olive oil which had been heated to 350 degrees Centigrade for ½ hour. The heat destroyed all the cholesterol according to Roffo. The fats under this treatment presented absorption spectra resembling those of the carcinogenic hydrocarbons. He believed the tumors to be due to the action of a carcinogenic oxycholesterol.

Widmark tested for the presence of cancer producing substances in roasted foods by painting mice every 2 days with alcoholic or petroleum ether extracts of such substances. He used horse meat heated to 275 degrees Centigrade, browned butter, and roasted coffee. No malignant tumors were recorded in male mice with extracts either of roasted or unroasted foods. Adenocarcinomas of the breast were present in 9 of 23 female mice which survived 11 months of painting with roasted foods (6 muscle, 2 coffee, 1 butter). The control series of 26 animals had only one breast carcinoma. The spontaneous tumor incidence for the strain was 10 per cent. He concluded that the extracts of roasted foods contained one or more carcinogenic agents.

Cook and Kennaway (24) were unable to confirm these experiments. They concluded that "as yet there is no convincing evidence of any specific dietary constituent in this connection." Roffo's work according to these investigators has not been supported.

In this connection, the work of Rowntree et al., who reported the production of spindle cell sarcomas in white rats fed an ether extract of crude wheat germ oil, has never been confirmed though many attempts have been made to do so. These experiments were unique at that time in that the neoplasms had arisen when the inciting agent had entered by way of the gastro-intestinal tract.

Kagawa claimed to have noted many stomach tumors in rats fed on "butter yellow" of Kinosita. The percentage was raised from 6 to 22 per cent when cholic acid was given simultaneously.

Tumors of the genito-urinary apparatus also have been induced by subcutaneous injections of betanaphthylamine. Papillomas, which graded from benign pedunculated types to infiltrative, sessile malignant ones were present on the base of the bladder. These tumors were first noted after 20 months in those dogs which had received fairly large subcutaneous dosages of the drug daily. Thirteen of 16 survivors showed pathological lesions (63). Degenerative changes were present also in the tubular epithelium of the kidneys and the parenchyma of the liver. There was also an anemia. Papillomas were discovered in the bladders of white rats treated with 4 oxy 2:3 dimethylazobenzol (100).

Sempronj and Morelli showed that beta-anthraquinoline had weak carcinogenic action on the kidneys of white rats given subcutaneous injections of this substance. Two of 8 animals which survived 11 months had adenocarcinomas of the kidney.

It has been known that teratomas of the testis of the rooster can be produced by injection of the gonads with a 5 per cent solution of zinc chloride in the spring of the year. Falin found that he could get similar tumors of embryonic character by the injection of 10 per cent zinc sulphate. The zinc salts formed albuminates, a caustic action being their primary effect. Areas of limited focal necrosis could be identified. In the immediate vicinity, the first tumor cells could be seen. Gonocytes seemed to be stimulated by a combination of the necrotic tissues and the active spermatogenesis of the spring season. Champy and Lavedan observed that partial removal of the testis of roosters was followed by regeneration from the fragment which remained. In 15 fowls which had repeated partial castrations over a period of 3 years, 4 developed huge tumors. These were malignant seminomas and embryomas. Apparently, the repeated active regeneration sufficed eventually to initiate the neoplastic response.

Many other experiments have been made with varied materials as inciting agents for neoplastic growth. Different types of animals also have been tested. A few of the most notable of such experiments can be cited. Passey reported that dogs which had been tarred weekly from 18 months of age, developed tumors after 6¼ to 6½

years. One of these was a malignant melanoma. Spontaneous tumors have been frequent in old dogs but this report shows that a long latent period must be expected in this species.

Selbie injected thorotrast into rats and mice. Tumors occurred in 25 of 43 animals 1 year or more old; 21 of these were spindle cell sarcomas, and 3 were fibromas. In 9 mice of 60 injected, there were sarcomas. These could not be transplanted in autotransplantation and homotransplantation. Foulds used young female guinea pigs to test thorotrast. He injected 0.2 to 0.3 cubic centimeter undiluted into the base of the nipple 4 times. They had carcinomas and sarcomas after 138 days. These tumors were transplantable and he carried them through 15 generations. These two observations are very important since thorotrast had been used rather freely formerly as a diagnostic agent. The danger of such a radioactive metal thus has been amply proved.

Although there has been difficulty in repeating Fibiger's rat stomach nematode neoplasm results, apparently a new parasitic nematode of the East Indies may prove to have this relationship. Bonne and Sandground discovered these parasitic worms in the hypertrophied tissue masses of gastric lesions in Javanese monkeys. They considered the growths to be adenopapillomas, some of which invaded the submucosa and showed aggressive possibilities.

Takizawa produced sarcomas in mice by daily subcutaneous injections of concentrated glucose solutions for over 1 year. Galactose and fructose were also successfully used but the percentage of tumors was less. He was not successful with lactose and sucrose. Suntzeff, Babcock and Loeb (133) were able to induce sarcomas in mice by injecting them 6 times weekly with hydrochloric acid (0.25 c.cm.) kept at hydrogen-ion concentration of 5. It took 10½ months.

The recent direction of experimental studies has been toward finding how the carcinogenic chemicals produce their effects. Experiments with tissue cultures afforded an opportunity to observe what happened to the cells directly exposed to solutions of these agents. Magat, Lebenson, and Volkeson studied the effects of 1:2:5:6 dibenzanthracene on mouse and fowl tissues *in vitro*. The hydrocarbon penetrated the cells in from 2 to 18 days. No changes were noted in the rate of cell growth or in the cell metabolism. They concluded that this hydrocarbon did not provoke inflammatory growth or cell proliferation.

Earle and Voegtlin found that methylcholanthrene and dibenzanthracene, even in high dilutions, caused severe growth retardation and degeneration in cultures of rat and mouse fibroblasts. The damage was roughly proportional to the concentration of the reagent and to the time of exposure. In no instance was growth stimulated by either hydrocarbon.

Owen, Weiss, and Prince determined that dibenzanthracene caused stimulation of cut segments of flat worms (Planaria) and regeneration of the whole animal. Triphenylbenzene, on the other hand, had no effect on the segments though it stimulated reproduction of the whole animal. Glutathione gave results similar to dibenzanthracene but some amino-acids had no demonstrable action.

Hollaender, Cole, and Brackett regarded the toxic effect of methylcholanthrene on yeast in cultures as a finer test for the dilution of this chemical than either the chemical or fluorescence methods.

Graffi could visualize with the fluorescence microscope the passage of carcinogenic agents into the cytoplasm of benign and malignant cells *in vitro*. He did not think that the nucleus was involved. The mitochondria seemed to have a selective affinity for these carcinogenic hydrocarbons. He suggested that the carcinogens act by deranging the cell metabolism through their effects on the mitochondria rather than by attacking the chromosomes.

Creech described an increased cell proliferation in cultures of mouse fibroblasts with some concentrations of carcinogens and a decreased cell growth with others. There was a precocious separation of the chromosomes in the prophase and metaphase with some of the carcinogens.

When paramecia were exposed to high dilutions of 3.4 benzpyrene for long periods of time, Mottram (96) was able to identify large abnormal individuals. If these were segregated he had abnormal strains which consisted of individuals many times the normal in size, or midgets, or Siamese-twin types. These aberrations could be maintained through many generations. Only a few of the exposed cells presented these changes but once they had taken place they were reproduced for many generations after the carcinogenic agent had been removed. The changes occurred among the cells long stimulated to a growth rate above the normal by exposures to the hydrocarbons.

Gey, after keeping tissue cultures of rat fibroblasts exposed to these artificial conditions for years, was able to transplant them into animals. Thus the production of sarcoma *in vitro* has at length been accomplished.

The action of the carcinogens on living cells seems to be an initial retardation of growth. It can be altered by changing the concentration of the chemical and the time of application. Apparently, after long application of dilute solutions, changes may be effected in cells so that they become abnormal. Such abnormal cells breed true and can be maintained as such in the absence of the inciting agent. The change does not appear to be in the chromosomes.

The initial retardation of growth was an unexpected finding with the carcinogenic hydrocarbons in tissue cultures. It was verified quickly, however, by experiments on transplanted tumors. Haddow and Robinson (57) used several well known transplantable animal tumors and tested the influence of various carcinogenic hydrocarbons against their growth rates. Retardation was immediate, prolonged, and relatively constant. The growth of the animals themselves was retarded as well. Also their fertility was reduced.

The same growth retardation effect was found to be true for spontaneous tumor growth rates (55). Dibenzanthracene and other carcinogens usually caused a prolonged retardation of growth. Sometimes the tumors partially or completely regressed. Some supposedly noncarcinogenic hydrocarbons produced the same effect. Later, they were shown to be weakly carcinogenic. Noncarcinogenic hydrocarbons produced a transient response or none at all. The prolongation of the retardation after the cessation of injections seemed to be an effect characteristic of carcinogenic compounds. It may be attributed to a toxicity of a special and possibly a specific kind.

It was even apparent that tumors induced by a chemical carcinogen could be retarded by injection of another though these tumors were less susceptible to inhibition than either the transplanted or spontaneous tumors (56).

In an elaborate experiment 34 compounds of known carcinogenic power and 34 supposedly noncarcinogens were tested for inhibitory action on both transplanted and spontaneous animal tumors; 86.5 per cent of the carcinogenic compounds showed inhibition of growth, whereas 79.7 per cent of the noncarcinogenic compounds showed no trace of inhibition. This association of growth-inhibiting properties and carcinogenic activity appeared to be statistically highly significant. The relationship between these two qualities did not seem to be quantitative since some feeble carcinogens had marked inhibition power (58).

Lees gave single subcutaneous injections of 1:2:5:6 dibenzanthracene to young rats. He found a prolonged inhibitory effect on their growth. It was not due to interference with their food consumption or to change in their metabolic rate. Nearly half of the animals died in 64 days. Other phenanthrenes including methylcholanthrene and 1:2 benzpyrene gave only temporary growth retardation. Jensen rat sarcoma was inhibited by 1:2:3:4 dibenzanthracene injections but the effect was less marked than that on normal tissues. Pollia could not concede a specific inhibitory effect of 1:2:5:6 dibenzanthracene on a transplantable rat sarcoma because he had inhibition from other noncarcinogenic agents. Appel et al. recorded a more rapid growth, more extensive and earlier metastases from Brown-Pearce rabbit carcinomas in animals treated with 1:2:5:6 dibenzanthracene than in the control group. The Whites pointed out that both carcinogenic and noncarcinogenic hydrocarbons retarded growth if given in the diet in adequate amounts. This varied widely with the substances used. There was a specific deficiency of the sulphur containing amino-acids in these animals. This may be related to an increased demand for organic sulphur as a detoxifying mechanism. Supplementary feedings with l-cysteine or dl-methionine caused a prompt stimulation of growth in these rats. Taurine, sodium sulphate, and glycine were ineffective. When McJunkin and Wolavka made intraperitoneal injections of an aqueous suspension of 1:2:5:6 dibenzanthracene and lecithin into rats, a transplantable rat sarcoma regressed completely in 20 of 51 animals. In many of the others the growth was slowed. Intratumoral injections were less efficacious. This tumor had resisted various other substances. Bauer reported that 7 humans with skin cancers remained healed over 2 years after the lesions had been injected with 0.5 to 1.0 cubic centimeter of a 0.5 per cent solution of 3:4 benzpyrene in ether. Twenty-two patients were treated by this method.

Some evidence has been accumulated that hemolytic activity may be one of the factors in carcinogenesis. All the strongly positive carcinogenic compounds possessed this quality on testing, while the negative compounds did not seem to have it. Confirmation of these facts has been obtained by a quantitative analysis of the iron deposited in the lymph nodes. In some experiments with carcinogenic agents there was a progressive increase in the lymph node iron to four times the initial figure (143).

Many of the carcinogenic hydrocarbons revealed a photodynamic action. There was a possibility that this might be correlated with the neoplastic

activity. But after a considerable amount of investigation this type of light sensitivity cannot be considered as of significance in connection with the carcinogenicity of the hydrocarbons.

Wolbach studied the tissue responses to carcinogens applied to the skin, subcutaneously, and to the viscera. Benzpyrene in benzene was used for the epidermal painting, cholesterol pellets of dibenzanthracene for subcutaneous implantation, and "butter yellow" in the food for the liver. All three chemicals proved to be destructive agents. A constant reparative process was maintained, involving repair of the damage to individual cells. Replacement of cells by division of adjacent ones also occurred. Hyperplasia was brought about by this mechanism. The injurious effects on the cells continued even during the stage of hyperplasia. These reparative responses in the regions of hyperplasia seemed to represent the stage preceding the development of true tumor. No direct chemical stimulation of cell growth was apparent.

Rondoni (122) used noncancerous substances subcutaneously. Nodules of connective tissue reaction were apparent. Regressive changes took place and there was no evidence of malignancy. Mixtures of cholesterinized liver had greater numbers of necrotizing substances so that the reaction was more intense and regressed more slowly. The sarcomatous changes from benzpyrene were first indicated by the appearance of multicentric abnormalities in the histological structure of the granulation tissue. Irregularities in the size and staining capacity of the nuclei were characteristic findings. A new race of sarcoma cells arose from the continuous action of the hydrocarbon on the labile undifferentiated cells of the reaction tissue, most likely a mutation.

Hval conducted experiments regarding the local tissue changes following subcutaneous injection of dibenzanthracene in mice, lard being the vehicle carrying the chemical. Lard alone caused a local hyperemia for a few days, then a cavity surrounded by fibrous tissue with no degenerative changes. Lard with neosalvarsan was followed by a more intense reaction which lasted for 6 weeks and then returned to normal. A cavity was left, lined by a syncytium and surrounded by connective tissue. Lard with the carcinogenic chemical gave changes according to the concentration. The local reaction was intense and persisted. It appeared to be irreversible if the dosage was sufficient. Degeneration and regeneration went hand in hand until finally regenerative cells began to assume more and more atypical forms in small foci. Mitoses were frequent. The cells seemed to be intermediate between macrophages and fibroblasts, at least they were mesenchymal with increased powers of development.

The lymphatics in acute and in chronic inflammatory lesions of mice were examined after injection with hydrokollag, a graphite preparation. Pullinger and Florey were able to demonstrate that the lymphatics were patent and unobstructed in tarred skin before and after the appearance of papillomas. The injected fluid reached and entered most of these warts. There was no sign of chronic lymphangitis. There was no overgrowth of endothelium into the lumen. Large dilated lymphatics were shown at the growing margins of 11 malignant tumors. Lymphatics were found in the center of only 1 tumor but failure to show them was not taken to be conclusive proof of their absence. The authors concluded that lymph stasis and obstruction were not essential factors in the production of benign tumors of the skin of mice.

Brunschwig, Tschetter, and Bissell (14) investigated the effect of 1:2 benzpyrene on rapidly proliferating epithelium. This was done by producing an ulceration in the painted areas. In one group radium was used for this purpose and in another, the actual cautery. The trauma was instituted at different time intervals from the beginning of the painting. Multiple papillomas and carcinomas occurred in all the animals. In spite of repeated applications the wounds healed and tumors did not arise in the newly formed epithelium.

Dietrich excised skin from mice painted with tar or benzpyrene. Small fragments were taken from the treated areas and from distant zones. The wounds were left open and 12 days later other samples were removed. The treated areas exhibited thickening, papillomas or atypical growth according to the duration of the painting. On the other hand, the distant sites showed only those regenerative changes present in unpainted controls. No indication was given that tar or benzpyrene induced a constitutional change favorable to the development of malignant growth.

Page applied a 0.3 per cent solution of methylcholanthrene to the skin of 3 to 4 months old white mice, 3 times a week. There was an immediate increase in the size of the cell, nucleus, and nucleolus, the most marked change being in the nucleolus. Squamous cell carcinomas appeared within 7 weeks in this group. With benzene alone there was no change in the nucleus or nucleolus. The average nuclear and nucleolar areas in the carcinomas were greater than those in the hyperplastic epithelium of the animals in which carcinoma did not develop.

Orr (107) tested the effects of six carcinogenic hydrocarbons, ten noncarcinogenic hydrocarbons, and a group of unrelated irritants on the skin of mice. Benzene and acetone were used as the solvents, but acetone was more satisfactory as it had no effect on normal mouse skin. The carcinogens produced early epilation, with regeneration of hair, abnormal in character. Progressive thickening of the skin, loss of elasticity, and passive congestion preceded the appearance of the tumors. The significant changes before tumor growth were considered to be: transformation of collagen into a fine fibered, nonrefractile type, first of the superficial but later of the whole dermis; passive congestion of the subcutis; alterations of elastic tissue in texture but not necessarily with an increase in amount; and absence of inflammatory cell infiltration. Small scars were found on the subcutis. The sites of tumors were related to these scars in a significantly high proportion. Elastic tissue hyperplasia was patchy, often with gaps at which tumors also appeared. The passive congestion probably caused an oxygen lack in the cells. The writer suggested that cancerization of epithelial cells by carcinogenic hydrocarbons was partly the result of changes in the deeper tissues. The mechanism in all probability was related to an interference with nutrition.

In a later study Orr (108) investigated the subcutaneous tissue responses. Pellets of paraffin wax containing 2 per cent carcinogenic hydrocarbons were introduced subcutaneously in mice. The animals were killed from 1 to 387 days later. With wax alone, there was a firm collagenous encapsulation within 2 months and no further change. With noncarcinogenic material in the wax, this capsule was thicker and longer in forming. When carcinogenic hydrocarbons were present, the initial reaction was the same but encapsulation was imperfect, the collagen being loose in texture and small in amount, with fibrinoid material on the inside. At a later date, cellular proliferations were found outside the collagen zone and at a distance from the pellet. The cells were of histiocytic and lymphocytic type and were the cells from which the sarcoma developed. These cells from which the carcinogen produced tumors were not present until a comparatively short time before the tumors appeared. Then, they collected outside the range of action of the carcinogen. The appearance of sarcoma in these cellular foci was apparently the result of a progressively increasing rate of division in an effort to provide an adequate fibrous capsule around the foreign body.

Brock, Druckery, and Hamperl placed benzpyrene in collodion sacs intraperitoneally. After a lapse of 8 to 12 months tumors appeared suddenly. All were sarcomas and in none could the agent be demonstrated by ultraviolet light. These growths appeared to develop at the periphery of the capsule where the concentration of benzpyrene was lowest and cell death accordingly had not taken place.

When rabbits were employed, no tumors could be made to arise at the site of direct application of 1:2:5:6 dibenzanthracene. Intravenous, subcutaneous, intramammary, intratracheal, and direct vaginal applications were made and no tumors appeared at any of the local sites within 900 days. The carcinogen had a slower action on this species but tumors were produced at sites remote from the application. Adenocarcinoma of the uterus, cholangioma and cirrhosis of the liver were noted. Burrows and Boyland (18) contrasted this peculiarity of the response of rabbits to the regularity with which tumors appeared at local sites of contact with this hydrocarbon in rats, mice, and fowls.

Efforts have been made to determine whether local acute or subacute inflammations might be effective in causing earlier localization of a carcinogen and consequent earlier tumor production. Rondoni and Corbellini (123) used a combination of painting with carcinogenic hydrocarbons and light cauterization of the area. They believed that the cauterization acted as a local realization factor. This precipitated the neoplastic development in a tissue potentially malignant from the application of the carcinogens.

Burrows, Mayneord, and Roberts (19) produced inflammatory foci in rabbits by the injection of kaolin and finely powdered silica suspended in olive oil. Each focus was given a single x-ray treatment of 600 volts. Twelve animals were started. The effective total was 9 of which 6 had tumors from 22 to 38 months following irradiation. Two tumors were of uncertain pathology but 4 were sarcomas. The probable rôle of chronic inflammation was to bring about a concentration and retention in the affected tissues of the specific agents of cancer.

Beck tested the influence of acute and subacute inflammation by combining turpentine with 3:4 benzpyrene in various ways to control the results. He made subcutaneous injections into mice. All groups injected with benzpyrene developed tumors. Fluorescence could be demonstrated in these tissues for approximately 6 months. Neither acute nor subacute inflammations had any effect on the development of sarcomas. The sarcomas

did not originate from the fibrous tissues of subacute inflammation.

Woglom used rats to test the effect of trauma on the localization and development of benzpyrene induced tumors. He soaked threads in a benzene solution of this chemical over night and then passed them through the viscera, kidney, testis, uterus, liver; 381 animals lived from 157 to 630 days and 29 had tumors about the threads in the connective tissue. There were no tumors in any of the organs. The glandular epithelium did not have its resistance lowered by benzpyrene by this relatively gross trauma.

Mottram (97) painted mice with benzpyrene in benzene for 75 days. Then 1000 r gamma irradiation was followed by a greater number of epithelial tumors than in the controls. If doses destructive to the epithelium were used as Cramer did (14,000 r to 18,000 r β-rays) the epithelial tumors were inhibited under the same conditions.

Mottram (98) continued this research by painting mice with benzpyrene long enough to produce warts. Then, a single dose of β-radiation was given. Benign and malignant tumors both appeared. All the tumors were in areas receiving from 800 to 2800 r. None occurred in areas receiving less than 800 r, and none arose under the radium applicator when the dose was 6000 r.

Kidd and Rous injected papilloma virus (Shope) into the blood stream of rabbits whose ears had been tarred 1½ to 3 months previously. This stimulated the growth of the tar warts with the production of squamous cell carcinoma.

Brunschwig (15) painted rabbits' ears with benzpyrene 3 times a week for 120 to 375 days. One out of 40 developed a carcinoma at the two hundred and twentieth day. In a smaller group of 19 animals treated similarly, but injected with extracts of human warts, 2 developed cancer. He concluded that on occasion the human wart virus might hasten the malignant degeneration of benzpyrene warts.

The possibility that the process of carcinogenesis might be related to some chemical reaction involving the carcinogen has been a stimulus to investigators. The general effects have been more difficult to unravel as the chemistry is involved and perhaps the agents were present only in minute traces. Sobotka and Bloch made lipoid extracts of 2100 liters of pooled urine from cancer patients. There was no positive chemical or biological evidence for the presence of carcinogenic hydrocarbons. They were able to detect small quantities of dibenzanthracene and phenanthrene added to 100 liters of normal urine so that the method seemed adequate.

There must be attempts of the tissues to eliminate these agents. Some evidence has been obtained by Dobriner, Rhoads, and Lavin following injection of 1:2:5:6 dibenzanthracene into rabbits, rats, and mice. The urine and feces were examined for any derivatives and the phenolic fraction of the excreta from rabbits gave an absorption band not present in normal animals. It was also not that of dibenzanthracene. A crystalline substance was obtained from this fraction. It proved to be noncarcinogenic for mice.

Chalmers injected mice intravenously with colloidal solutions of 3:4 benzpyrene, methylcholanthrene, and cholanthrene. The fluorescence spectra of the bile, urine, and feces were examined. After benzpyrene was injected, the bile showed a spectrum different from that of benzpyrene due to some substance (named B P X) insoluble in ether. There was a substance also in the feces probably identical with B P X. A second substance in the feces was ether soluble and had a spectrum differing from B P X. The urine gave a general fluorescence, not banded. The same was found to be true for all the excreta following the injections of methylcholanthrene and anthracene.

After intraperitoneal injections in lard or colloidal watery solutions of 1:2:5:6 dibenzanthracene into mice, only 40 per cent could be demonstrated by fluorescence 12 days later. Within 3 weeks almost all the lard injected material had vanished and only ⅓ of the colloidal material remained. The delicacy of this test made it apparent that the mouse was able to metabolize this carcinogen. The hydrocarbon suffered rapid alteration in the animal body. Some chemical reaction occurred which exhausted most of the carcinogen before tumors began to appear (41).

Hieger could not detect by fluorescence spectroscopy the carcinogenic hydrocarbons in extracts of mouse and rat skin 4 weeks after their last application.

Reggiani, Dansi, and Morelli after intravenous injection of 3:4 benzpyrene in rats found that extracts of the liver gave an absorption spectrum different from that of benzpyrene.

Intravenously injected benzpyrene in mice was retained by the body fats, and excreted as an altered substance in the bile. The colloidal benzpyrene could be found in the blood serum, the central nervous system, and the sebaceous glands. Some pregnant mice had this hydrocarbon in the placenta but it could not be found in the fetus. Traces were found in the milk from lactating breasts of mice (Chalmers).

Other changes of a general nature have been observed by Lewis. Certain tumor bearing animals had a severe neutrophilia in the peripheral blood and a myeloid hyperplasia of the spleen, bone marrow, and lymph nodes. In them, areas of myeloid infiltration were found in the adrenals.

Similar systemic effects were noted by Parsons. The picture of the lymph nodes was similar to that from lethal or sublethal doses of x-rays. Twort and Twort observed a correlation between hyaline degeneration and enlargement of the spleen and the carcinogenicity of the agent applied.

Congo-red has been removed from the circulating blood of normal rabbits at a definite rate. After painting the animals with carcinogenic hydrocarbons for a year this normal removal rate tended to disappear (Hoch-Ligeti).

Roffo (120) claimed that when cancer of the skin was induced in white rats by the influence of sunlight, it was due to a concentration of cholesterol in the skin. This compound was then rendered photosensitive by the ultraviolet irradiation it received.

Mayneord and Roe found that cholesterol, previously irradiated with ultraviolet light, x-rays, β- or γ-rays from radium produced an appreciable blackening of the photographic plate in the vicinity. The effect also could be obtained by prolonged heating. It could not be brought about *in vacuo*. They believed that probably an unstable ozonide or peroxide was formed. No evidence of an absorption spectrum resembling any of the carcinogenic hydrocarbons could be found although 40 specimens irradiated under different conditions were examined.

Bergmann et al. studied the effects of the application of irradiated cholesterol to the skin of mice. Neither benign nor malignant tumors were produced though the treatment was extended over a period of 2½ years.

Schmid injected 0.2 per cent irradiated ergosterol in linseed oil into the gall bladder of guinea pigs. The cystic ducts were ligated. The animals were sacrificed in from 3½ to 9 months and though the glandular elements had penetrated into the submucosal tissues, no true tumors were found. Perhaps the elapsed time was not sufficient.

Buengeler experimented upon three groups of mice with photosensitive substances. Eosin, hematoporphyrin, and tar in dilute solutions were injected subcutaneously twice weekly. The animals were exposed to sunlight daily for 4 to 5 hours over a period of 210 days. There was a high mortality. The reaction could be divided into three types. In the early weeks acute inflammation was manifested by conjunctivitis, dermatitis, eczematous skin reactions, vesiculation, and ulceration. In a later period after 2 months there was a progressive loss of hair, atrophy of the epidermis, mast cell infiltration, and a hypertrophy of the connective tissue. From 3 months on tumor formation was apparent. It was a gradual imperceptible change from the proliferative process. At first the tumors were benign—papillomas and fibromas. But after 6 months many of the tumors became malignant. The tumors were multiple usually. Squamous cell carcinomas and spindle cell sarcomas were the commonest forms of malignancy. Myeloid leucemia and tumors in the lung were also noted. Degenerative changes were present in the organs; as well as amyloidosis; and hemorrhagic necroses of the gastric walls.

Taussig et al. tried the effect of light on benzpyrene painted mice. They found no significant differences between the tumor incidence in the dark, light sensitized, and light kept mice.

Rusch and Baumann irradiated mice daily with a mercury quartz light. Papillomas, epitheliomas, and spindle cell sarcomas were developed on the ears in from 35 to 82 per cent. These tumors could be transplanted. Their incidence was lower in black mice. Irradiation for long periods was productive of more tumors than short period irradiation. A high fat diet produced tumors most rapidly, cholesterol had no effect when added to the diet. Brain and liver in the food caused retardation in tumor production. In the rat, Roffo's observation of increase in the cholesterol content of the skin by ultraviolet irradiation was confirmed. But in the mouse and guinea pig there was no increase under these circumstances.

Doniach and Mottram (35) showed that the skin of white mice painted with carcinogenic hydrocarbons became sensitive to blue violet rays of the visible spectrum. They demonstrated that the skin under these conditions became red and edematous.

Morton, Luce-Clausen, and Mahoney (94) found that white mice of the Swiss albino Bar Harbor strain kept in the dark and painted with 0.5 per cent 3:4 benzpyrene in benzene twice weekly for 17 weeks developed a much higher percentage of carcinomas over the next 2 months than a similar group kept in visible light. Ultraviolet light was excluded. These results indicated that the carcinogenic agent 3:4 benzpyrene could induce skin tumors in mice in total darkness. Ordinary light apparently had a retarding action on the carcinogenic process.

Doniach and Mottram (36) confirmed these observations. They pointed out that though tar and benzpyrene produced a greater dermatitis in the light, light is not essential for tumor production. They painted mice with benzpyrene and cholanthrene, purified in the dark. Tumors were produced in the skin of mice by both agents though the mice were kept in total darkness. The effect of darkness was to reduce the dermatitis to a minimum. There was no inhibition of tumor production or hair growth. The effect of strong sunlight upon the similar chemically painted skins of mice was to increase dermatitis and to reduce tumor production. Perhaps this action was due to the photodynamic properties of the hydrocarbons. The cells which took up the chemicals were sensitized to light and many of them have been seriously damaged or killed.

These observations fit with the biological effects of light upon plant life. It is known that light exerts an inhibiting effect on the growth of plants. The growth is much more rapid in the dark. It is at its maximum rate just before sunrise. Sprouting is therefore carried out in the dark by many agriculturists. The heliotropism of growing plants is partly due to the greater growth rate of the stem away from the light.

Lacassagne's demonstration that estrogens had carcinogenic properties inciting mammary cancers in mice led to much activity in this line of investigation. The work was confirmed and extended in many laboratories. The hormones had an appeal to the investigator as they were normally occurring growth stimulators and not chemical substances unlikely to be encountered in the animals. They were shown to have specific effects on the genital tissues. They became available in purified, concentrated forms.

Methods of administration have been worked out. Subcutaneous injection has been used most commonly. The estrogens have been dissolved in various solvents such as benzene, oils, chloroform, alcohol. Pellets of the substances have been implanted for long, slow action. Local applications to epithelium or injections into organs or tissues have been employed. The substances have been given orally but although not impaired by digestion, the method has been less effective. Intraperitoneal injections have been carried out.

Estrogens have been demonstrated in many tissues in the human—the ovaries, placenta, blood, urine, bile, feces, etc. The hormones may be rapidly destroyed, probably by the liver in an oxidation process. After oral or hypodermic administration, about 20 per cent has been excreted in the urine or feces. The estrogens disappeared rapidly after intravenous administration. The urine of humans of both sexes and at all ages has been shown to contain female sex hormones, possibly indicating extragonadal sources of these secretions.

Some of the first work has been to define the normal physiological actions of the estrogenic substances. The studies of sex differentiation and the internal secretions has resulted in a brilliant advance in our knowledge of these complex relationships.

Only a few of the many excellent endocrine investigations in relation to cancer can be reviewed briefly here. It was demonstrated that male mice of high breast tumor strains could be made to develop mammary cancers by long continued injections of estrogens. Males from very low breast tumor strains could not be influenced in this way, but females of the strains have been made to develop tumors after very prolonged estrogenic stimulation (11).

A 6 years' summary of the effects of weekly injections of estrogenic hormones on 6 pure strains of mice showed that mammary cancers occurred only in those strains in which they developed spontaneously. They were present in larger numbers and at an earlier age in the males as well as the females in the susceptible strains. Sarcomas were noted at the injection sites and often around the oily cysts in some of the mice. No spontaneous sarcomas were seen in these strains (Lacassagne, 68).

Sarcomas developed in 10 of 247 mice injected with ovarian hormones over long periods of time according to Burns et al. The growth seemed to start suddenly in contradistinction to the step by step gradual change when carcinomas arose.

Nelson reported that, when guinea pigs were given estrone in oil for 2 to 10 months subcutaneously, fibromyomas of the uterus and adenomatous hyperplasia of the endometrium were observed. In the cervix there was metaplastic downgrowth and pearl formation.

Loeb et al. (79) were unable to find any precancerous or cancerous changes in the uterus of 300 mice injected with estrogens though some showed penetration of the uterine glands into the muscle and metaplasia of the epithelium.

Gardner et al. (46) reported "the first convincing demonstration of a malignant cervical tumor induced by estrogen" in mice. The previously observed epithelial hyperplasias of the cervix were probably also precancerous. This tumor was grafted successfully into male and female mice of the same strain. The tumor grew rapidly without further estrogen stimulation.

Loeb et al. (80) believed that estrogens affected the stroma of organs in two opposite directions. By inducing growth processes of the epithelial structures the amount of hyaline fibrous material in certain organs—vagina, cervix, uterus—may be diminished. Or, if large doses were administered over long periods, the opposite was obtained—marked increase in fibrous and hyaline material in the stroma similar to the changes of old age. Suntzeff et al. (134) showed that this hyalinization of the uterus was reversible when the estrogen injections were stopped. The mammary glands continued on to cancer indicating that here the stimulus could become manifest many months after the estrogen had ceased to act.

When 4 pure lines of mice had been receiving estrogenic hormones, a considerable number of lymphosarcomas were noted. Eleven of these originated in the thymus. No mice of these strains had such tumors spontaneously in 5 years of observation (Lacassagne, 69). This has been confirmed by Gardner (47).

Robson and Bonser induced mammary cancer in male mice of a susceptible strain by weekly injections of a synthetic estrogen, triphenylethylene. Lacassagne (70) did the same thing with another synthetic estrogen, diethyl stilboesterol. Geschickter used the latter agent which is not a sterol. He induced cancer of the breast in 1 rat. Mammary cancers were obtained in 26 others with estrone. This strain never had spontaneous cancer of the breast.

Gardner, Strong, and Smith (50) found that the mammary glands in mature female mice of strains of high susceptibility to spontaneous tumor development had more localized nodules than those of the low tumor strains. These nodules were made of hyperplastic, resting, or regressing glandular tissue. If normal factors were responsible for them, there must be additional local factors to account for their localization.

Van Gulik and Korteweg could not determine a great difference in the estrous cycles of high and low strain tumor mice. But there was a difference in susceptibility to follicular hormones, some strains requiring more to affect them than others. The genital organs of the two high breast cancer strains were less susceptible to follicular hormone than those of the three low breast cancer strains. Under normal conditions the females whose genital organs were least affected produced the greatest quantity of follicular hormone.

Wolfe (150) studied rats for a comparison of estrous cycles, fertility, and tumor incidence. The strain with low fertility was associated with a high tumor incidence.

The possibility that overtreatment with estrogenic substances was responsible for a cancer of the breast in the human was suggested by Auchincloss and Haagensen.

The mammary glands of the monkey have proved resistant to estrogenic stimulation. The Yale group has worked for 5 years on this species with negative results to date.

The pituitary gland has been caused to undergo changes following long continued estrin injections. Marked enlargement of the anterior part may be seen especially in rats. There may be intense congestion. The entire gland may be almost entirely chromophobe cells with practically complete absence of acidophils. Definite adenomas in the rat have been produced by Wolfe and Wright (152) and Zondek among others. The latter investigator noted a retarded growth and inhibited sexual development as well. The pituitary tumors had the same amount of gonadotropic hormone as the normal pituitary animals. This suggested that it was not the production of the hormone but its utilization that was inhibited. Lacassagne (73) could not see a correlation between the hypophyseal changes and cancer susceptibility in 4 strains of mice treated with estrogens. The pituitaries varied from no change to adenomas, sometimes malignant. Perry (114) had pituitary tumors in 3 of 131 mice receiving estrone treatment.

Turner and Gomez (138) were convinced from their experiments that production of mammary tumors in male mice of susceptible strains by the long continued application of ovarian estrogens was effected by way of the pituitary—a mammogen being responsible.

Loeb and Kirtz (78) transplanted anterior lobes of hypophyses into inbred strains of mice. This caused marked development and secretory activity in the mammary glands of these strains. An increase in the cancer rate in virgin mice was noted as compared to that in similar virgin mice without the hypophyseal transplants. Cancer could not be induced by this means in the low cancer strains. Presumably the effect was from increased production of estrogen in the ovaries because of these transplants.

Lacassagne (72) could not cause development of the mammary glands in male mice which had been hypophysectomized though he injected them with estrogenic substance for 152 days. Male mice of a high breast cancer strain R 111 were injected weekly with estrone benzoate. When a marked degree of hyperplasia of the breasts had been established, hypophysectomy was carried out 2 or 3 months later. In spite of

continued treatment with the estrogen, the breasts rapidly atrophied. When carcinoma of the breast had been induced by estrone, hypophysectomy caused only temporary regression with resumption of the growth.

The adrenal gland has reacted to estrogen treatment as well. Cramer and Horning (29) painted mice for 5 to 6 weeks with estrin. Both sexes showed a brown degeneration of the zona reticularis into the medulla. This was found in spontaneous high mammary cancer mice also. It was always fully developed before cancer appeared.

Dobrovolskaïa-Zavadskaïas and Pezzini (34) did not regard this association of brown degeneration and cancer formation as significant, but thought it related to an endocrine disturbance. They had mice with it, without cancer, and vice versa.

Cramer (28) believed that in spontaneous cancer the adrenal medulla was affected, whereas in induced estrogenic cancer, the zona reticularis outside the medulla was involved.

Woolley, Fekete, and Little ovariectomized mice at birth. In these animals the adrenal cortex took over the hormonal functions of the ovary enough to bring about a normal development of the uterus and mammary glands. In high mammary cancer strains it could even lead to carcinogenesis in the mamma.

Gardner and Pfeiffer (49) showed that while bone was being resorbed from the pubic region in mice under estrogen treatment, it was being deposited in some of the long bones, almost obliterating their marrow cavities.

Lacassagne and Raynaud (74) injected mice of R 111 strain with testosterone twice weekly from 1 to 20 days after birth until death of the mice. The mortality was high. None of the mice which lived developed mammary carcinoma. The normal incidence of this strain has been 60 to 70 per cent in the females. The mammary glands did not develop, which may have been the reason for the absence of mammary cancer.

Wolfe and Hamilton (151) inhibited or reduced the incidence of mammary tumors by a simultaneous injection of androgens with optimal doses of estrogens for tumor production. Flaks and Ber inhibited the induction of methylcholanthrene cancers by large doses of testosterone. It was necessary to apply minimum doses of the chemical and maximum doses of the hormone to get this effect. Maisin et al. could not increase the incidence of tumor in mice receiving applications of benzpyrene to the skin and simultaneous injections of testosterone. No tumors developed at the site of injections.

In male breast hypertrophy Hoffman has had some successful regression following testosterone therapy. Anterior pituitary hormone therapy was without effect.

Pybus and Miller noted that spontaneous bone tumors in their mice occurred 2½ times as frequently in males as in females. They also were present 2½ months earlier.

Marine and Rosen presented evidence that lymphomatosis in their fowls was closely associated with a deficiency of male hormones. This was manifested by absence of comb growth in all 16 and absence of testicular tissue in 11. In the remainder, there were atrophic fragments of testis. All birds which developed the disease were typical capons.

The androgens can be administered to humans by mouth without clinical benefit although a much smaller dose intramuscularly will be effective. The hormone was not passed out in the feces, but absorbed from the intestine into the blood stream and eliminated by the kidneys (Dorfman and Hamilton).

The melanin pigment formation in the human skin may be related to the androgens and to the hormones of the adrenal cortex.

Larionow was unable to demonstrate any morphological alterations in the ovary, testis, thyroid, thymus, parathyroid, suprarenal, hypophysis, or pancreas in mice painted with benzpyrene. He concluded that it was not by way of the endocrine system that the action of carcinogenic compounds was effected. This did not exclude their participation in the process of origin in spontaneous tumors.

Von Haam and Cappel studied the various hormonal effects on fibroblasts *in vitro*. Estrin was a slight growth stimulator, progestin had a remarkably inhibiting effect, testosterone was inhibiting, thyroxin was moderately stimulating in proper concentration. Insulin caused an unmistakable increase in growth—as much as 10 times the normal with rapid accumulation of fat droplets and transformation of the tissues at the margin into fat cells. Adrenalin deteriorated rapidly. It was an inhibitor. Cortin was also a pronounced inhibitor.

Narimatsu inhibited Kato rabbit sarcoma growth by large doses of posterior pituitary lobe hormone. Anterior gonadotropic hormone gave a similar result; growth hormone from anterior lobe accelerated tumor growth. Complete or incomplete extirpation inhibited the growth, as also did irradiation of the pituitary by x-rays.

Moppett thought that implanted tumors were stimulated by extracts of the anterior lobe con-

taining both growth and gonadotropic hormones. Thyroxin on the other hand retarded the growth.

Bischoff and Long were unable to influence the onset or incidence of adenocarcinoma of the breast in Marsh-Buffalo mice by the injection of prolan. The ovaries underwent an enormous hyperplasia and presumably a marked hyperovarian function resulted.

Druckery produced no effect on transplanted tumors by prolan injections. Earlier work showed castration to have inhibitory effects on transplanted tumors.

Ball and Samuels found that the growth of Walker rat tumor 256 was much slower in hypophysectomized male rats than in those controls fed an equal amount by stomach tube. Control tumors were 3.3 times as large at end of 3 weeks. The change in tumor growth was abrupt, indicating a direct effect of the removal of pituitary secretion. Adrenal cortical extract had no effect. Atrophy of adrenal cortex cannot be held responsible.

Ovarian castration inhibited the appearance and evolution of tar induced tumors in rabbits (Tavares and Morais).

Benzpyrene was estrogenic for mice in doses between 4 milligrams and 31 milligrams (Perry, 113). Sarcoma produced by benzpyrene stopped the estrous cycle when grafted subcutaneously in rats but the cycle was resumed upon the removal of the grafts (Halberstaedter and Back).

From these studies it may be gathered that the hormones have a definite part in carcinogenesis. The interaction of the various glands of internal secretion serve to confuse the parts played by each one. The genetic factors must also be taken into consideration. These seem to vary from strain to strain and there can be no doubt that some factors are extrachromosomal in inheritance.

The demonstration of a breast factor by Bittner may be an explanation of part of the difficulty. He showed that first generation mice from high breast cancer strains when foster fed by mothers of low cancer strain had a low cancer incidence. When the opposite experiment was done, the reverse was true. Something was passed to the sucklings from the mother's milk which modified their future tumor incidence. This means that in the development of mammary cancer in mice, the investigator must take into account the genetic factor, the extrachromosomal factor, the foster nursing factor, perhaps the functional activity factor as well as the hormonal one. This latter in itself, may be the result of an interplay between several hormones. The reason for localization of cancer in one breast must depend on some local peculiarity. The anatomical development of the breast is regulated by the pituitary and the ovarian hormones. When the breasts have been developed to certain stages step by step through cyclic proliferations and regressions, after a sufficient latent period, the genetic behavior of these organs can be demonstrated (Lacassagne, 71). The intrinsic factors may be overwhelmed by the administration of estrogens over long periods no matter what the normal reaction would have been. This overthrow of inherited resistance is similar to that produced by any other inciting agent such as x-rays. The evidence at present seems to be against an antagonistic action of male hormones or at least their action is feeble. Similarly, progesterone has little if any effect on the development or stimulation of mammary tumors. Whether there are other factors so that there is a synergistic action between adrenal cortical hormone and estrin with thyrotropic pituitary hormone as antagonist to these two, with perhaps adrenal medulla as another antagonist (Cramer, 28) must remain for future investigation. At any rate it remains true that, "we are completely ignorant as to the mechanism whereby estrone produces cancer of the breast in the mouse" (Dodds as quoted by Gardner, 48, in his excellent review of this subject).

Whereas estrin acts mainly on the breasts, it has been shown to have effects on the cervix for cancer induction as well. Sarcomas have arisen at the injection sites. And lymphoid malignancies have been noted. Cystic endometrial hyperplasias, metaplastic changes in the uterus and pyometra have been frequently observed. Hypertrophy and myxomatous transformation of the connective tissues of the cervix and vagina have been noted. Bone resorption of the pubis and overproduction of bone in the long bone shafts have taken place. Adenomas of the pituitary gland were seen by many observers. Thus, the action of this hormone is more widespread than it was formerly thought, when it was supposed to be confined to those tissues for which it was a normal stimulant.

The other hormones, in a like manner, are being more extensively studied. Better preparations are available. There can be no doubt that their place in carcinogenesis will be clarified in the next few years.

Before hastening into print with remarkable new discoveries, it would be well for some investigators to study the historical development of cancer research. In the early years, it was known to all cancer workers that animals which were sick or undernourished were unsuitable for cancer

experiments. Only the very healthy animals were used because the others would not grow cancers. A few tumors which were demonstrated after manipulation with potent chemicals were not considered significant especially if the normal cancer incidence of the animals was not known. It has become increasingly evident that some of the highly susceptible mouse tumor strains have latent tumor possibilities which can be lighted up by almost any inciting agent. In such cases, one must be exceedingly cautious in his conclusions.

CONCLUSIONS

The number of known chemical carcinogenic agents is large. There is no evidence that a definite chemical structure is necessary for carcinogenic activity. These chemicals vary from simple acids and alkalis (HCL, NOH), metal salts ($ZnCl_2Zn\ SO_4$), radio-active compounds (thorotrast), sugars (glucose), to complicated dyes (dimethylaminoazobenzene), hydrocarbons (3:4 benzpyrene, 1:2:5:6 dibenzanthracene, methylcholanthrene), estrogens (complicated sterols), and viruses (heavy proteins).

Methods for testing the carcinogenic action of the chemicals have been evolved by careful laboratory investigations.

The "average time" required for tumor production is that which is required to produce tumors in about one-half of the animals tested.

The "effective total" is that number of animals which is still living when the first tumor appearance is observed.

The "maximum effective" or "limiting dosage" is important as an indication of the quantity of the carcinogenic agent to which the tissues can show a response. The limiting dosage varies from species to species.

There is an intrinsic factor for cancer susceptibility or resistance handed down in inheritance. This factor may not necessarily be genic, but extrachromosomal at times as well. Pure strain animals make possible better controlled observations.

Sex and season should be taken into consideration. Also the vehicle-solvent may not be disregarded.

The known life histories and spontaneous tumor incidence are important.

The carcinogens may unmask the latent spontaneous potentialities of the strain. Certain chemical carcinogens seem to have selective action on certain tissues.

Epithelial growths, sarcomas, and visceral carcinomas can now be induced by chemical means.

Different species have tendencies toward different types of tumors. Each species has its own characteristic tumor rate, organ susceptibility, and latent period. It varies with the strain.

The carcinogenic chemicals have a toxic action. Locally, they damage the tissues so that the reaction to them is imperfectly developed. Their initial effect is one of growth inhibition. The damaged tissues may release substances which modify the neighboring cells much as Spemann's evocators do. The cancerization appears to originate in the region but not directly at the site of application of the carcinogen. All the strongly positive carcinogenic chemicals cause some hemolysis. Most of the powerful carcinogens have a photodynamic action. But light is not essential for tumor production. The chemical carcinogens undergo metabolic changes in the body.

In attempting to detoxify these chemical agents, the essential sulphur containing aminoacids may be used up. Some of the carcinogens are changed in the liver and intestine giving different fluorescence spectra than the originals. They are eliminated as sulphonated and phenolic compounds in some cases. There are general systemic effects following their application noted in the blood, lymphoid apparatus, vascular system, and kidneys.

This process may be considered as one of physiological aging. In young animals the carcinogens precipitate the changes toward senility. Tumor age is shortened (Murray, Mider and Morton, 95).

The hormones are naturally occurring potential carcinogens. Under ordinary circumstances their functions are physiological regulation. In repeated forced action they may become potent carcinogens. The estrogens may be rapidly destroyed by oxidation in the liver. They are excreted in the urine and feces.

Many hormones are synergistic with or antagonistic to other hormones. They can be studied by accentuation of their normal action or by complete removal of the organ responsible for them. Under such circumstances overdevelopment of certain organs may occur; or atrophy.

Cancers may be induced in the overdeveloped organs or prevented by not having an organ to function.

The process of cancerization still remains a mystery in its final steps.

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NEUROGENIC SARCOMA

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THE term sarcoma imparts a distinct and well understood meaning. The word neurogenic creates the thought of arising from nerve tissue. When these two words are put together implying a name, inaccuracy and probably confusion results. Sarcoma must originate from tissues that have a mesodermic origin. Nerve tissue begins in another layer, the ectoderm. Hence, the inaccuracy of the title. Furthermore, the recognized source of neurogenic sarcoma is from the sheaths of the central and peripheral nerve trunks or fibers and not from nerve tissue. However, the title, though oddly coupled, has the advantage of being well established. It also creates in our minds two valuable ideas: first, the disease is malignant; second, it specifies the geography of the disease, the areas and structures where such an entity might be suspected.

We, as clinicians, may properly overlook discrepancies in terminology, once they are understood. Our task is to become familiar with the etiology, symptomatology, and therapy of an interesting subject, neurogenic sarcoma.

The etiology of neurofibromas, neurofibromatosis or von Recklinghausen's disease is unknown. So too is the cause of neurogenic sarcoma unknown. All of these arise from the connective tissue coverings of nerves. There are some who believe that neurogenic sarcoma always arises from the sheath of Schwann. The embryological origin of this sheath compared to the origin of the other coverings of nerves, cranial or peripheral, and the tumors which arise from them has been thoroughly discussed by Penfield, Stout, and Geschickter.

Many are of the opinion that a solitary tumor called neuroma or neurofibroma may be a single manifestation of a disease which at times is capable of producing multiple tumors. And further, postmortem examination may reveal that there had existed a fibromatosis involving hidden nerve tissue. The author suggests that one who wishes to familiarize himself with the interesting subject of neurofibromatosis in a comprehensive manner should obtain Thomson's monograph, *Neuroma and Neurofibromatosis*.[1]

Neurogenic sarcoma has been found in practically every area and organ of the body. Such extensive distribution of a disease not only signifies its importance but increases the multiplicity of signs and symptoms that can accompany it. The alertness of the clinician is ever necessary if diagnostic errors are to be avoided. It must be admitted, however, that few of these tumors are properly labeled prior to exploration or biopsy, and then often with difficulty. The reasons apparently for mistakes with this disease are: First, it is not common. No doubt it is more frequent than suspected. Second, its rarity naturally causes the observer to direct his attention to the organ producing the symptoms—stomach, intestine, lung, brain, spinal cord. Third, intracranial or motor and sensory symptoms, pain included, suggest a more frequent condition than neurogenic sarcoma. The visible or palpable tumor calls to mind a more common type of lump.

It must not be inferred that just because skin manifestations are not present, a visible or palpable lump cannot be a sarcoma of nerve sheath origin. Many occur, though diagnosed as a more frequently seen tumor and operated on as such, followed frequently with recurrence.

CASE 1. C.S., No. 53,581, a white woman, aged 43, was seen January 6, 1938. The patient was referred to us because of a tumor of the upper left side of the chest. She said this began as a birthmark which was a flat red spot about 2 inches wide. She also said that there was a spot on this red area which seemed to be a wart, which 17 years before had been opened by accident. Bleeding occurred. It began to grow larger following this injury, and after 3 years was operated upon and supposedly removed. On January 21, 1924, the pathological report described a myomatous growth on shoulder, soft and microscopically on border line between myoma and nonmetastasizing spindle cell sarcoma. She also had an abdominal operation at this time. Two years later, the growth was about the size of a walnut and was again removed by the same surgeon. On July 6, 1926, the pathological report described a subepithelial proliferation of fibrous tissue with much production of collagen typical of keloid. Five years ago she had a thyroidectomy and the recurrent tumor was again removed by another surgeon. No pathological report was obtainable. Two years ago, she noticed the tumor growing again. She had lost some weight. She had been dieting.

On examination we saw on the anterior portion of the left shoulder (Fig. 1) a growth and also a scar. Both

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[1]The Surgeon General's Library of Washington, D.C., was kind enough to loan the author a copy of this book through the King County Medical Library, Seattle.

Fig. 1.

Fig. 1. Case 1. The tumor began as a birthmark. It was removed three times, recurring after each operation.

Fig. 2.

Fig. 2. Case 1. Gross specimen removed with cautery. Skin graft was necessary.

measured about 12 by 5 centimeters. This was a large tumor 5 by 3 centimeters, and raised above the level of the skin 4 centimeters. There was a bluish cast to the most prominent part of the mass. Behind this and above it was a reddish spot which seemed incorporated in the scar. At the lower margin of the scar, there was another reddish area which seemed more like a growth. It was slightly tender. The rest of the scar was white. The scar was movable on the chest wall. There were no enlarged nodes in the axillary, cervical or supraclavicular areas.

At operation the tumor mass including all of the surrounding scar was dissected widely down to the fascia of the pectoral major muscle (Fig. 2). The fascia of that muscle was removed with the circumscribed tissue. Several large vessels were encountered approaching the mass in the subcutaneous tissue. These were ligated at a distance. The cautery was used throughout. The wound could not be closed, hence the area was covered with a pinch skin graft.

In microscopic sections of this nodule there was a section composed of collagenous, firm, fibrous tissue, moderately vascular, enclosing the nodule described grossly. This latter was composed of haphazardly arranged bands and whorls of reticular fibers packed with cells, the margins and cytoplasms of which were indefinite, but the nuclei were prominent, round or spindle-shaped. Some of the nuclei were larger and more active than others but in no place was there any evidence of malignancy.

Diagnosis: "Fibroma. Sections stained with Masson trichrome technique and with van Gieson, show that there is much collagen material between the fibroblastic type of cells. This is a fibromyoma and can be called a neurofibromyoma, but it is not a nerve sheathed tumor" (Fig. 3).

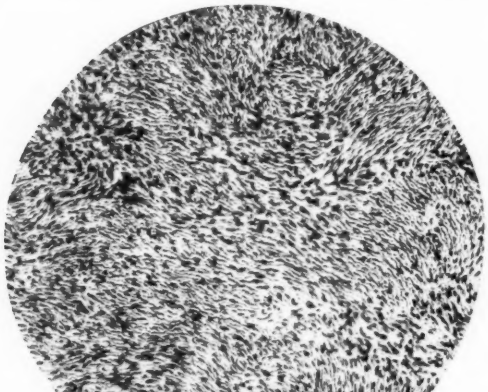

Fig. 3. Case 1. Photomicrograph of a fibromyoma or neurofibroma.

This case apparently was not microscopically a neurogenic sarcoma, but its repeated recurrence shows that it was clinically malignant.

CASE 2. F.G., No. 65,081, a white male, aged 55, was seen August 9, 1934. The patient came to the clinic with a tumor of the right upper arm, inner side. It had been gradually increasing in size. He first noticed this lump by accident 4 or 5 years ago. A year ago, he noticed a kind of numb pain with itching of the hand. There had been a stinging pain in the arm since last April.

The patient presented a tumor on the under surface of the upper arm that encroached upon the posterior axillary fold. It was about 14 centimeters in length and 7 centimeters in diameter. It was fairly soft and slightly tender. It was more tender when one pressed it upon the under surface of the arm along the level of the nerves and vessels than it was from bilateral compression. It was rather soft and compressible. When the patient was directed to have the triceps muscles put under tension, this tumor came markedly to the surface and became hard. There were no palpable nodes in the axilla. The grip of both his hands was about the same. We were unable to recognize

Fig. 4.

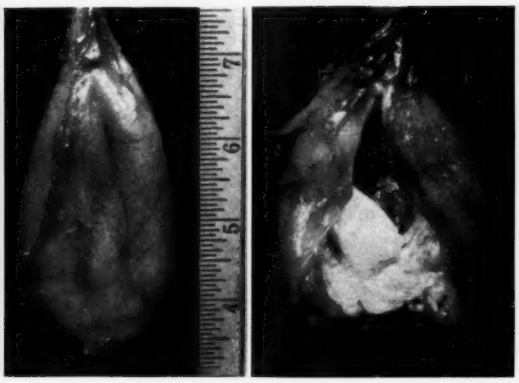

Fig. 5.

Fig. 4. Case 2. Age, 55 years. The patient first noticed a lump 4 or 5 years ago on the under side of the upper arm. A year ago, he noticed pain with itching of the hand. The tumor is 7 centimeters in length and 5 centimeters in diameter. It is fairly soft and tender. It is more tender when one presses upon the under surface along the level of the nerves and vessels than it is on the opposite or posterior surface. It is soft and compressible. The tumor was removed June 11, 1934, with cautery. The pathological report was neurofibroma, benign. He has been seen recently with no evidence of recurrence.

Fig. 5. Case 2. Gross tumor involving the radial nerve.

a difference in pulse. The mass did not pulsate. The tumor was removed.

At the operation, it was found, after the tumor was exposed, that a large nerve entered the proximal end of the tumor as shown in Figure 5, but its identification was lost in the tumor wall; however, it emerged as a nerve strand distal to the tumor. It was necessary to sacrifice this nerve. The patient has been seen recently and there is no evidence of recurrence.

A diagnosis of neurofibroma, benign, was made August 11, 1934 (Fig. 4, 5, 6).

Pathological report: This is a soft, egg-shaped structure, 15 centimeters long and 7 centimeters in diameter. It is covered with a smooth sheet of membrane-like tissue and from it, apparently incorporated in the wall, are several cord-like structures resembling nerves. Sectioning reveals the structure as a cyst-like formation with a soft wall from 0.5 to 1 centimeter thick, composed of soft, quasi-translucent, pale yellow-brown tissue. To the lining are adherent small collections of glistening, greasy, semicrystalline yellow-brown material, and the cavity contains about 50 cubic centimeters of thick, greasy, glittering, pale-yellow fluid.

Microscopic examination revealed adherent to the lining a much necrotic, largely amorphous material arranged in a pattern of many angular clear spaces, from which some crystalline material has presumably been dissolved out; microscopic examination of the fluid content revealed cholesterin crystals. Beneath the lining, the wall was formed by dense fibrous tissue, in places hyalinized, in places heavily infiltrated with lymphocytes and plasma cells. Deeper still the tissue was of much softer texture and formed by small round and oval cells with nuclei about 10 microns in diameter, surrounded by clear spaces and a small peripheral membrane so that the general pattern was that of nerve tissue; these cells resembled myelinated nerve fibers; interlaced with them in many places were thin spindle cells resembling fibroblasts. There was also in this part of the wall a heavy infiltration of lymphocytes around some of the blood vessels. Nothing resembling ganglionic cells could be identified.

Finding a single neurofibroma of a large nerve trunk prompts the constant watch for the appearance of others.

The literature is replete with caution (Adair, Pack, and especially Ewing), to the surgeon that the removal of such a tumor requires preparation for radical surgery. Nerve roots entering or attached must be severed with a wide margin to avoid recurrence. Stewart has called our attention to the fact that extension from the tumor

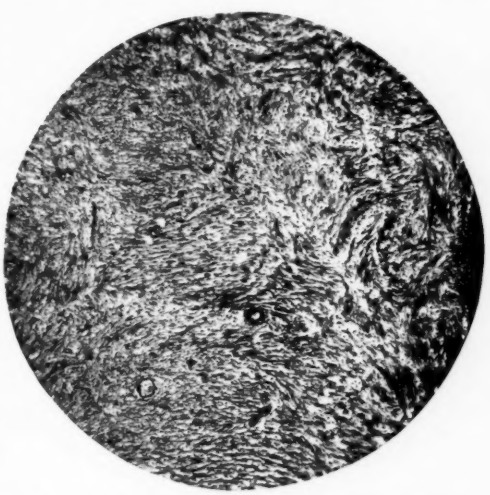

Fig. 6. Case 2. Photomicrograph of a neurofibroma.

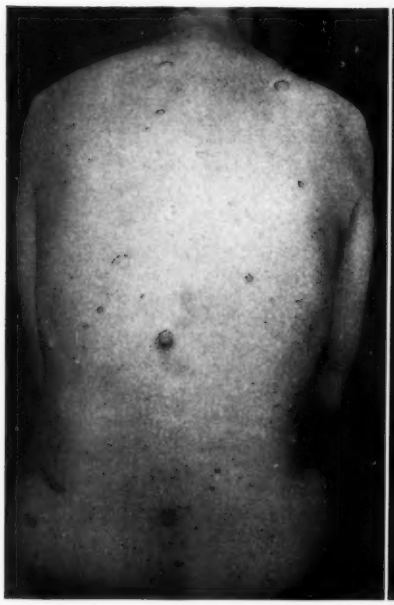

Fig. 7.

Fig. 9.

Fig. 7. Case 3. Over the patient's body were scattered discrete papilloma-like tumors which arose from the skin. None were pedunculated. She stated that she has had these all her life. They were compressible and tender.

Fig. 9. Case 3. We found a tumor mass on the inner side of the left leg at the level of the left knee joint, of which the patient complained. This was a smooth, globular tumor mass 16 centimeters in diameter which had localized tenderness. There was a brownish color over it which was similar to other spots on her body. This mass was firmly attached to the structures of the internal surfaces of the knee joint. The mass was quite firm, compressible and partially movable. There were areas of pigmentation all over the body. These areas were of different size.

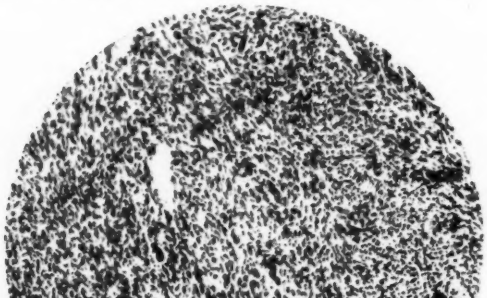

Fig. 8. Case 3. Photomicrograph of tumor seen in Figure 9. Neurogenic sarcoma.

may readily proceed within the nerve sheaths some distance from its origin. The nerve trunk may not be larger than normal, but it should be severed far beyond the growth. Large blood vessels similarly associated with the growth are ligated as far away as possible.

Multiple neurofibromas are more commonly found on the surface of the body. They are variable in size. The shape usually is spherical or ovoid. They may be pedunculated or sessile. Some are palpable in the deeper layers of the skin. The newer ones apparently are pinkish in color, while the older ones take on the color of the surrounding skin or are paler as if time had deprived them of the blush of young vascularity. The surface of the skin in these individuals is usually pigmented, ranging from that of small freckles scattered indiscriminately to larger, rounded, and irregular patches of darker or light brown color. The great majority of these abnormalities are painless.

The history records that these tumors be-

Fig. 10.

Fig. 10. Case 4. The patient, aged 66, has multiple tumors over the skin of the body. Two months before coming to the clinic in September, 1933, one posterior to the right ear became ulcerated and increased rapidly in size. It had been cut by his barber several months previously and had not healed.

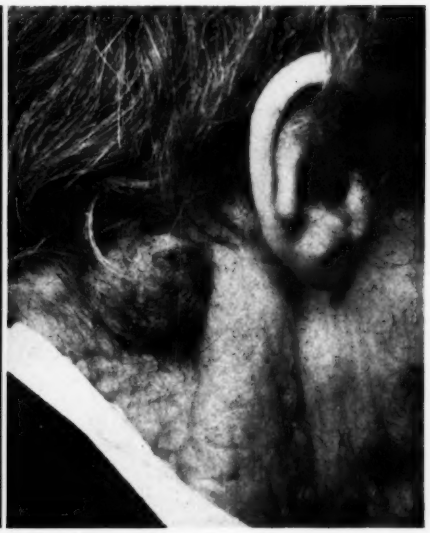

Fig. 12.

Fig. 12. Case 4. Generalized skin manifestation of von Recklinghausen's disease. One growth on the neck ulcerated.

gan in early childhood and have gradually increased in number and size as the years passed. The patient has become accustomed to his abnormal skin, and he considers it not worthy of complaint.

Many observers (Ewing) have mentioned that accompanying the skin manifestations of this disease, occasionally neoplastic changes exist on deeper nerve trunks. They may involve both motor and sensory groups. Pain or other sensations naturally follow the involvement of tracks which are sensory in nature. Craig emphasizes this symptom.

One of our patients (Case 3) was seen because she began having the appearance of a lump and pain, although for years, there had been multiple lumps in her skin.

Case 3. E.A., No. 22,039, a white woman, aged 42, was seen March 3, 1932. The patient had a swelling of the inner surface of the left knee. The swelling had become painful, radiating to the foot. She noticed a mass about 1 year ago and it had grown since then.

Examination revealed over the patient's body scattered discrete papillomatous-looking tumors which arose from the skin. None of the papillomas were pedunculated. She stated that she had had these all her life. They were compressible and tender (Fig. 7). We found a tumor mass on the inner side of the left leg at the level of the left knee joint of which the patient complained (Fig. 9). This was a smooth, globular tumor mass 16 centimeters in diameter which possessed localized tenderness. There was a brownish color over it which was similar to other spots on her body. This mass was firmly attached to the structures of the internal surfaces of the knee joint. The mass was quite firm, compressible, and partially movable. There were

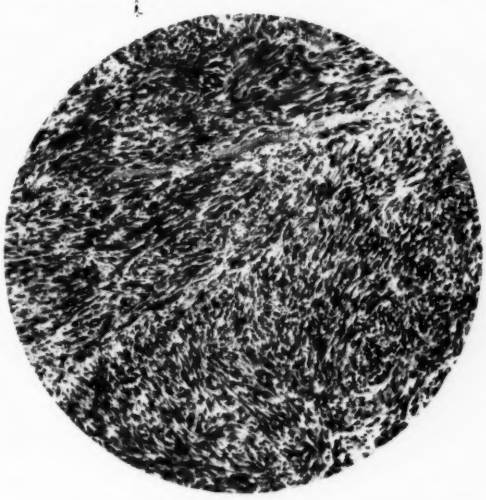

Fig. 11. Case 4. Neurofibroma or neurogenic sarcoma.

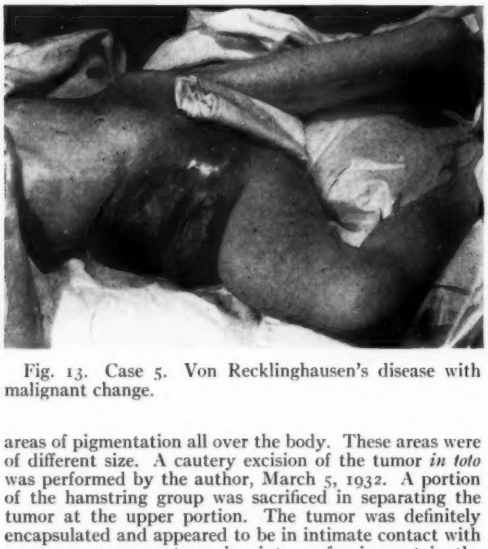

Fig. 13. Case 5. Von Recklinghausen's disease with malignant change.

areas of pigmentation all over the body. These areas were of different size. A cautery excision of the tumor *in toto* was performed by the author, March 5, 1932. A portion of the hamstring group was sacrificed in separating the tumor at the upper portion. The tumor was definitely encapsulated and appeared to be in intimate contact with a sensory nerve root passing into or fraying out in the tumor. On subsequent visits, there was found lymphedema of the lower leg which disappeared later. When last seen 3 years later, there was no evidence of recurrence.

At operation was found a tumor of the leg, 15 centimeters in diameter, thinly encapsulated. On one side the capsule was firmly adherent to the muscle fascia. On bisection, the central portion consisted of putty-like necrotic material. The tumor substance was soft, friable, and actively proliferating at the surface. The gross diagnosis was necrosing sarcoma (Fig. 8).

Microscopic examination showed that the tumor consisted of moderate sized spindle cells and fairly numerous mononuclear giant cells. Mitosis was prominent.

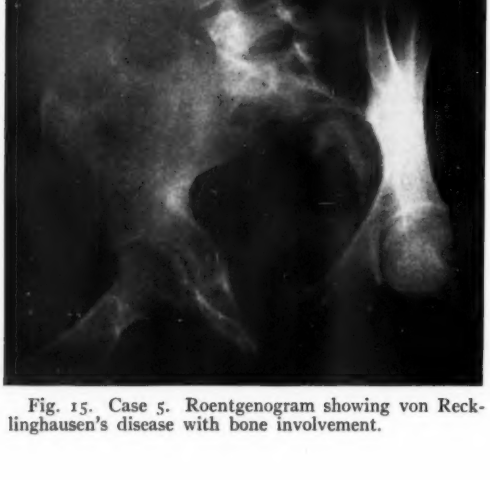

Fig. 15. Case 5. Roentgenogram showing von Recklinghausen's disease with bone involvement.

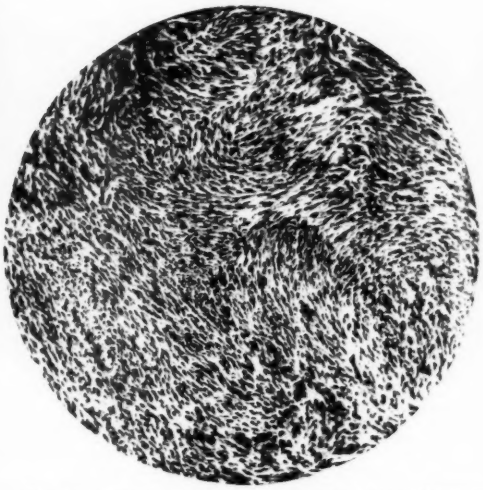

Fig. 14. Case 5. Von Recklinghausen's disease showing neurogenic sarcoma. One of the multiple tumors was removed to complete the record. It was a neurofibroma.

Diagnosis: Possible rhabdomyosarcoma, or neurogenic sarcoma.

On August 19, 1933, a tumor was found over the twelfth thoracic vertebra. A small piece of tissue was removed from the back. The piece of skin was 4.5 by 2 centimeters in size. In the center of it was a papillomatous growth 1 centimeter in diameter. Immediately underneath this papillomatous growth was a tumor mass 1 centimeter by 2 centimeters.

The diagnosis was neurofibroma. (Taken to complete the record.)

The lump, interestingly enough, of which the patient complained, was fortunately superficial and palpable. Had it arisen from a nerve trunk more deeply situated, and had she not had skin manifestations to offer a clue toward a diagnosis, she doubtless would have been subjected to a number of imaginable procedures for diagnosis, emphasizing again the statement that symptoms with pain which are not diagnosed by modern procedures may (with merit) suggest this disease.

This patient had neurogenic sarcoma associated with von Recklinghausen's disease. She was seen 3 years later with no evidence of recurrence. Such a patient should be informed by her physician that her disease may again produce a tumor of malignant type.

The most important clinical significance of von Recklinghausen's disease is that malignant changes do occur. This change may be exemplified by local recurrence following the removal of what was thought to be a benign tumor. The intimate association of such a lesion with a nerve should

warn the surgeon that the removal of this growth must be complete with a wide margin, else as has been warned by Ewing, Hosoi, and others, a recurrence is apt to appear, the eradication of which is more difficult and more mutilating than apparent at the first operation. Hosoi states:

"In résumé, malignant transformation takes place in about 13 per cent of all cases of von Recklinghausen's disease. When this happens, the tumor grows rapidly and tends to recur locally even after repeated operative measures. Metastasis is usually late and frequently absent, but may rarely occur early. In some cases, the mere extirpation of a malignant tumor or even a benign one appears to stimulate another neurofibroma distantly located to undergo sarcomatous transformation. Prognosis is very poor, the patient succumbing to cachexia and postoperative complications if not to the metastasis."

For emphasis, I further quote his remarks reporting recorded cases of malignant change in neurofibromatosis.

"According to Garre, there is a striking tendency to sarcomatous transformation in multiple neurofibromatosis, for in at least 12 per cent of all cases this sarcomatous change takes place from a benign neurofibroma. Garre calculated this percentage on the basis of 17 collected cases. . . . Using the 1927 figures of Fischer, when he collected reports of 466 cases of von Recklinghausen's disease, one obtains an incidence of malignant changes of about 13 per cent which is in agreement with Garre. These neurosarcomas have been observed more frequently in the deeper nerve trunks.

"Ewing stated that the serious nature of these deeper tumors is very imperfectly realized by most surgeons, so that the number of victims of this disease is much larger than is generally believed. He added that the primary attack on these tumors must be undertaken with great caution."

Adair's practical article on neurogenic sarcoma so frequently associated with this disease is one of the few which offers suggestions for the therapy of these tumors.

Westphalen reported a case of multiple fibromas of the skin, nerves, and ganglia, one of which in the fifth cervical nerve underwent a sarcomatous change.

"In their cases of [from Hosoi] multiple neurofibromatosis, Campana described a sarcomatosis of the skin; Sorger, a sarcoma of the axilla; Gernet, a sarcomatous transformation of a massive plexiform fibroma of the shoulder and upper part of the arm; Heydweiller, a fibrosarcoma of the right popliteal space; Feindel, a sarcoma globocellulaire of the leg; and Gluge, a sarcoma in the pelvis, the size of a child's head.

"In Cimmino's case, a large sarcoma in the sacral region was associated with about 450 fibromatous tumors of the skin. Jeanselme and Orillard reported a case of fibrosarcoma of the saphenous nerve with elephantiasis molle congenita of the overlying skin. Adrian found at necropsy a fibrosarcoma of the duodenum which was associated with multiple fibromas of the skin and internal viscera and a neuromyxoma in the supraclavicular fossa about the size of a child's fist. In MacKenzie's case, in addition to the multiple soft tumors in the skin, a good egg-sized sarcoma of the sciatic nerve was observed. Shouldice reported a case of multiple peripheral fibromas in which operation disclosed dozens of small tumors about the size of millet seeds all over the stomach and a fibromyxosarcoma on the greater curvature of the stomach."

Ten to fifteen per cent of neurogenic sarcomas are associated with neurofibromatosis—von Recklinghausen's disease—and are the ones most frequently diagnosed. The physician recognizes this association as an important clue. When, however, a deep seated tumor is found in such a patient, the thought—appreciating its location—that it might be a neurogenic sarcoma should be kept in mind, or if the tumor is superficial, larger than others, growing or producing symptoms, its diagnosis is more likely.

CASE 4. D.E., No. 52,659, a white male, aged 66, was seen in September, 1933. The patient had multiple tumors of the skin (Fig. 10). Two months before, one posterior to the right ear had become ulcerated and increased rapidly in size. It had been cut by his barber several months previously and had not healed.

At examination the patient complained primarily of a lesion behind his ear on the neck, which was 3 centimeters in diameter and raised above the skin for about 1.5 centimeters. It was hard, ulcerated and dry (Fig. 12). We noted over the entire body multiple lumps that were in the skin, varying in size from 4 centimeters in diameter down to pinhead dimensions. Some were distinctly pink, and some a little bluish in color. Those deeper in the skin had a bluish cast. The majority of them were on the abdomen and chest; fewer on the legs, especially below the knee. There were some on the feet, and some on the hands, even on the palms. There were none on the scalp.

The tumor on the neck was removed. It proved to be an ulcerated neurofibroma (Fig. 11). The patient did not return until November, 1934. At this time, there was a large stony-hard mass in the neck just anterior to the scar. He said that this mass had been present for 6 months and had become larger. He was having difficulty in swallowing food and could take only liquids. He had a constant cough, was greatly emaciated, and in a critical condition. He died shortly thereafter.

One must suspect that the tumor in the neck interfering with swallowing, breathing, and producing a cough, was of neurogenic origin. We are also forced to think that the surgeon who operated did not permit the multiple skin tumors to direct his trend of procedure. It is unfortunate that consent for a postmortem examination could not be obtained.

CASE 5. D.McK., No. 24,458, a white women, aged 25, was seen in November, 1939. When two years old, a small lump had appeared on the lateral side of the right buttock. This increased gradually in size and was removed surgically when the patient was 7 years old. At the same time, the patient had a similar lump on the right buttock which is the beginning of the present large tumor. Following this operation, a number of lumps appeared on the body, first on the left thigh. An attempt was made elsewhere 3 years

ago to remove a tumor of the right thigh, but the tumor was not completely removed. Pathological report was neurofibroma. It recurred. Since that time, the patient has been able to walk, although she had considerable pain in the right hip in March of this year. This pain had been present for at least a year and one-half and had become worse during the 3 months before she came to the hospital in November, 1939. She was unable to walk when first seen.

The details at examination were furnished by Dr. G. W. Kling who is now practicing in Centralia, Washington. The patient was emaciated and lying in bed with the right leg flexed 90 degrees at the hip and abducted 70 degrees. All of the skin was involved by cutaneous and subcutaneous nodules which were extremely soft and easily compressed. They varied in size from a match-head to the size of a walnut. The skin over the abdomen, legs, arms, and face was pigmented in patches of various sizes. She complained of considerable pain in the right ilium where a large tumor mass was present. Apparently, this large mass which comprised most of the right side of the abdomen arose from an attempted removal 3 years before of a tumor in the right thigh and inguinal region.

The left side of the abdomen, beginning about 6 centimeters to the left of the umbilicus was free of findings. The entire right side of the abdomen was involved in a tumor mass extending deep into the tissues and apparently attached to the right ilium. This mass extended from about 6 centimeters to the left of the umbilicus toward the right around to the sacro-iliac articulation; above, it extended to the costal margin and was limited below by the pubic bones. The surface of this tumor was raised about 6 centimeters above the normal contour and was rough, shiny, and red. The large mass consisted of two definite lobes. In the region of the pubic bones, the skin was exceptionally tight, and pain was produced by slight pressure. There was no area of ulceration, but the crevice between the lobes contained a small amount of caseous material (Fig. 13).

A small lesion was removed from the left hip for completion of our records. It proved to be a neurofibroma (Fig. 14). X-ray of the pelvic bones showed marked involvement of the right ilium (Fig. 15).

This was a typical case of multiple neurofibromatosis in which a neurogenic sarcoma involving bone had developed. It illustrates the disastrous results which accompany ill-informed approach to the surgical removal of a tumor, the clinical picture of which was plain. The pediatrician should have definitely in mind the significance of neurofibromatosis so that he can with justification tell the parents that while the disease is usually of no great consequence, yet it is apt to progress and may produce hidden symptoms when deeper lesions are associated, also that it can develop malignant changes. Parents or an older child when informed of the characteristics of this condition are prompted to ask, as the years go by, for consultations regarding the disease rather than be, because they have lived with it peacefully for years, totally unconcerned.

Such an attitude thus created by the pediatrician or general practitioner may be of great profit to the patient as well as to the profession. The patient is protected and the physician is trained to believe that one or two small lesions in the child might become multiple and therefore diagnostic in the adult. The progressiveness of the disease is emphasized for their attention. They also realize that it may advance to a point of real seriousness. Doubtless, in many instances this stage could often be obviated had the patient been informed.

SUMMARY

The clinical significance of a disease is increased by its frequency. The more people who have it, the more attention it receives. If, on the other hand, a condition is rare, its importance to the physician is reduced in proportion to its rarity. But each discovered instance of it creates definite interest. When a clinical entity, seemingly unusual, proves, by reason of its varied characteristics, to be more common than previously thought, its significance increases. But when the disease can be a malignant one, the challenge to us is greater. We, as physicians, are obligated to recognize in the benign, the rare possibility of the malignant and to see to it that ignorance on the part of the patient is not our fault. Multiple neurofibromatosis, like leucoplacia, deserves respect as well as watching. Neurogenic sarcoma is rarely diagnosed prior to biopsy or operation. When associated with neurofibromatosis, a clue is present.

The surgeon deciding to remove a tumor arising in soft tissue must be prepared to do a more radical resection if he finds nerve trunks entering the growth. The close association of neurogenic sarcoma to neurofibromatosis obligates the pediatrician or family physician to warn the parents of a child having that disease of its future possibilities.

The author wishes to express his indebtedness to Dr. Clyde Jensen, pathologist of the King County Hospital for his valuable interpretation of the tissue examined from these patients. The author also wishes to thank Miss Gertrude Egan for securing the case records and typing the article. He here expresses his appreciation to Mr. Martin Baker, the photographer of the King County Hospital, who is responsible for all the excellent photographs.

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RADIATION DAMAGE TO TISSUE AND ITS REPAIR

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THE roentgen-ray is a powerful physical agent. When it was first discovered its action was not well understood, and the dangers connected with its use were not realized. Much damage resulted, both to the physicians and technicians using it and to the patients. Its use at that time resulted in few cancer cures. Later, as its action became better understood and new measures were introduced for the protection of workers and patients, the damage resulting was reduced to a minimum. In this second era the greatest number of cures were of skin cancers. In many other types of cancer the roentgen-ray seemed at first to retard the growth but the results were not lasting. In other words, it almost cured cancer.

With the development of higher voltages and the use of larger dosages over long periods of time, we have all observed a striking improvement in the results. Now we see many cures in patients who a decade ago would not have been helped. However, we repeat that we are dealing with a powerful agent which may do great damage to normal tissues as well as to abnormal tissues. Radiologists are well aware of these dangers and rightfully expect assistance from the surgeons. Unless surgeons are able to repair damage from radiation, roentgenologists will not use intensive doses and they will not cure as many patients.

There was a time when many radiologists were afraid to cause erythemas or ulcerations of the skin for fear that the patient would accuse them of having "burned" him. If the situation is explained to the patient and, if he knows that his skin is going to get red and sore, there will be few legal complications.

In considering radiation damage to tissue we must distinguish between temporary and permanent changes. We must consider the early injuries and the late damage. We wish to know the degree of damage, whether the tissues are ulcerated superficially or deeply, edematous, fibrosed, or whether there is actual necrosis. Finally, we are interested in the late degenerative changes in the tissues and in the development of cancer in certain instances.

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The mildest form of radiation damage is the erythema or blush on the skin. All x-ray machines are calibrated as to the amount of irradiation necessary to give an erythema. Usually several times this erythema dose is used to destroy a lesion. A simple erythema may be followed by desquamation, a severe erythema by ulceration. Often the radiologist treating cancer produces an ulceration and thereby feels that he has delivered the maximum dosage possible. These reactions in the skin are accelerated, delayed, or prolonged according to the amount of treatment given daily and the total number of treatments. Modern technique is based on the fact that if the treatments are carried out over a period of from 2 to 4 weeks the treatments are more effective on the neoplastic tissue and the damage to normal tissues is lessened. Ordinarily the ulcerations of this type are ugly in appearance but give little pain and usually heal within a few weeks. If the patient is told what to expect he will have few complaints.

As much treatment as is necessary should be given during the first cycle before permanent changes appear in the tissues. Later the skin becomes thickened, edematous, and leathery, the blood vessels become narrowed and carry a decreased supply and there is fibrosis of fat and subcutaneous structures. Once these changes have set in, further treatment must be given with caution. The effect on the tumor will never be as great in a second series as in the first and the amount of damage to tissues already fibrosed will be greater. Painful, persistent ulceration may appear and this will require surgical measures to remedy it.

Infection entering an area previously heavily irradiated may cause extensive necrosis and sloughing of the area. Lesions in the mouth, pharynx, rectum, and bladder are particularly susceptible to infection after irradiation; the skin is not as fertile a field for infection.

Ischemia of tissues is the forerunner of necrosis. Patients with arteriosclerosis and the resulting endarteritis, syphilis, and diabetes may have such poor circulation that they tolerate irradiation poorly, particularly in an extremity. Irradiation of cancer in the tongue of a syphilitic is not so satisfactory, for undue sloughing appears.

Irradiation over an operative wound must be carried out cautiously. The elevation of flaps in

a dissection of the glands of the neck or a radical amputation of a breast may interfere with the circulation of those flaps. The extra burden imposed by roentgen therapy may be sufficient to cause death of the skin flaps.

Whenever irradiation is given through normal skin to an underlying cancer and the treatment is given in sufficient doses to destroy cancer, the normal skin and any other normal tissues in the path of the rays will receive permanent damage. This is an argument used by some for not giving "prophylactic treatment" after an operation for a condition which appears to be favorable. However, this fact should not be used to halt necessary treatment, for these damaged tissues can be repaired if late changes occur.

Irradiation reaction during the first few months after treatment consists in bronzing of the skin, endarteritis, and fibrosis of the subcutaneous tissues. This may not be severe enough to cause serious damage. However, if a large artery supplying this damaged area is ligated, complete necrosis of the entire irradiated field may develop within a few days. We have seen the same type of necrosis after an alcohol injection of the mandibular nerve for relief of pain.

Late changes in an irradiated field comprise telangiectases of the skin, followed by hyperkeratoses in the skin, alopecia, fissures, fibrosis of and later loss of the subcutaneous fat, marked endarteritis of the smaller vessels, and degenerative changes in the fascia. The extent of these late changes depends on the amount of irradiation originally given, the time interval and the region involved.

The most serious of all complications from irradiation is the development of cancer of the skin in the treated area. Ewing points out that there is an incubation time between the use of roentgen-rays and the development of cancer of from 3 to 11 years. The shortest incubation time we have seen is 2½ years and the longest 18 years. Roentgen cancer is usually of the epidermoid type. It is slow to metastasize but when it does, metastasis is rapid and extends at first in the lymphatics and finally in the blood stream.

The scope of this subject is so great that many types of injury can be barely mentioned and others not considered at all. All irradiation therapy is based on the theory that malignant cells are susceptible to doses that will not seriously damage the normal cells. That presupposes that we know exact extent of lesion to be treated which, of course, is not always true. Unfortunately, the depth of the treatment cannot be entirely controlled.

The mucous membranes of neighboring organs may be nearly as susceptible to the roentgen-ray as the tumor itself. It has been demonstrated by Warren and Spencer that permanent damage to the lungs may follow therapy to the breasts and chest wall. It is well known that irradiation of the uterus may produce ulcerations in the rectum and bladder as well as fistulas, and that intensive therapy over the intestines may cause ulceration. We have seen one pathological fracture of the femoral neck due to roentgen therapy of the inguinal nodes.

TREATMENT

Treatment of these injuries cannot be described in a paragraph. No two tumors offer the same problem, no two cases of irradiation damage can be handled in the same way. In general, it may be stated that treatment will be based on removal of tissues which are damaged beyond their own power of repair, on the relief from infection, on short-circuits to avoid continual irritation of an involved organ and in the replacement of tissues by free grafts or flaps. Treatment may be prolonged, but the relief afforded is so satisfactory to the patient that time is a small factor.

We have collected a group of cases illustrating the types of injury which we are meeting, and we have described the methods of repair used. These cases illustrate all degrees of permanent damage and include several which have shown late malignant changes.

Group I. The removal of superfluous hair by roentgen therapy. A decade ago it was common practice for certain beauty parlors to advertise the removal of superfluous hair by the "Tricho system." This treatment proved to be x-ray treatment, apparently given without adequate control of dosage. Four cases are cited; in 2 painful necrosis occurred and in 2 malignancy developed. It is probable that, if given enough time, cancer would have appeared in all these lesions.

Case 1. H. S., age 49, was seen on October 31, 1939. Fourteen years before he stated that he received x-ray treatment by the "Tricho" system for superfluous hair on both upper arms and shoulders. The hair disappeared and he had no trouble until 4 years before when, following a sunburn, the lesions began to itch very badly. He had been under observation by a dermatologist since then and there had been no suspicious areas until this examination.

Examination showed an area of irradiation dermatitis extending from just above the tip of the shoulder nearly to the elbow and covering a full half the circumference of the arm. In the center the tissue was very hard and in places nodular. Around the borders the skin was soft but showed marked telangiectases. It was felt that the nodular areas might be beginning malignancies and treatment by excision and graft was advised. The other arm showed the same condition without the induration (Fig. 1).

Operation was done on November 7, 1939, at the Baker Memorial Hospital. The area of dermatitis was excised. The subcutaneous fat was extremely indurated and it was

necessary to remove it down to the muscle. The defect was covered by several Thiersch grafts. The pathological report stated that irradiation dermatitis was present but no malignancy. "The microscopic sections show a diffuse dermatitis with slight keratinization of the epidermis, flattening of the papillae, and a dense acellular avascular fibrosis of the corium in which no hair follicles or sweat glands are noted. There is a moderate lymphocytic infiltration throughout and one section shows a localized superficial area of edema resembling a tiny bulla with polymorphonuclear leucocytes and narrowing of the epidermis in this region. The arterioles show slight subintimal proliferation."

CASE 2. E. G., Westfield Sanatorium No. 2,649, age 39, was admitted April 17, 1040. She states that she received x-ray treatment by the "Tricho" system about 9 years ago for superfluous hair. One year ago she noticed an ulcerated area near the angle of the mandible. This has increased in size and a recent biopsy showed epidermoid carcinoma, grade 1. On examination both cheeks and upper cervical regions showed generalized skin atrophy with telangiectases. In the center of the irradiated area on the left was an ulcer 1.5 by 0.8 centimeters which was obviously malignant (Fig. 2).

Surgical excision of the ulcer and part of the atrophied area was done and reported to be epidermoid carcinoma. She made a good recovery. It will be necessary to excise all the irradiated tissue in this patient as she will undoubtedly develop new malignant areas.

CASE 3. F. L., age 38, was seen in March, 1931. Several years before she had received x-ray treatment at London, for hair on her chin. A dermatitis developed and finally an ulcer on the chin. Examination showed a marked telangiectasis with ulceration and induration around the ulcer, suggesting malignancy. Excision was done at the Beth Israel Hospital in March, 1931. The entire area of dermatitis was removed and a segment of the mandible was chipped off. Later the defect was closed with a Thiersch graft. Unfortunately the specimen was lost and there was no microscopic examination but the gross appearance was that of cancer. At the time of operation no subcutaneous fat was found and none appeared to form beneath the graft following operation. She was followed for a number of years after operation and was very much dissatisfied with the appearance of the graft. The graft remained extremely white (Fig. 3) and she had great difficulty in using cosmetics to make her presentable. On several occasions the matter of removal of the graft and closure by flaps was suggested but as she had other surgical conditions which were more urgent this was postponed. It was later done, however, by another surgeon.

CASE 4. V. S., age 48, teacher, was seen on September 6, 1938. In 1925 she had received x-ray treatment by the "Tricho" system for superfluous hair on the legs. Three years later she noticed changes in the skin and these increased year by year. During the past year a dermatologist had given her 14 radium treatments without benefit to the affected area.

Examination showed a grayish, painful ulcer 4 by 3 centimeters over the calf of the right leg. The edges of the ulcer were raised and firm. Around the ulcer the skin showed telangiectases, induration, and a loss of subcutaneous fat. There were no palpable regional lymph nodes. A diagnosis of x-ray dermatitis with possible malignant change was made (Fig. 4). Operation and graft were advised.

Operation was done at the Baker Memorial Hospital on September 10, 1938. All the involved skin was excised and the deep fascia was removed. An immediate Thiersch graft was done. Pathological studies showed acute inflammation with necrosis, but no cancer was found. Areas of necrosis appeared in the graft but healing took place rapidly.

The characteristic features of these lesions are telangiectasis of the skin, dryness with itching, poor blood supply, and either changes in, or loss of, the subcutaneous fat. The treatment is always removal of the affected skin down to normal tissue. Radiation treatment for this condition, as was done in Case 4, should be condemned.

Group II. Roentgen therapy for dermatological lesions with late degenerative changes. The following cases are illustrative of this group:

CASE 5. M. M., age 68, was examined on June 19, 1934. She had had psoriasis for years, worse on the knees and elbows. Two and one-half years previously she received 3 x-ray treatments over the knees and 2 over the elbows at 1 week intervals. Five days after the last treatment the knees became black, swollen, and painful. The elbows were the same to a lesser degree. She had to go to bed because of pain and stayed there 7 months. The treated areas became raw and discharged constantly. Her doctor treated her with boric acid and electrotherapy, but this made her worse. She went to another doctor, who treated her with a special serum he obtained in Chicago. She had 10 injections of this at $45.00 a treatment with no benefit.

Examination revealed that both elbows and right groin had extensive radiation changes in the skin but no ulceration. Both knees showed similar radiation changes with central deep ulceration 3 inches across. The left ulcer showed 1 area of new-growth (Fig. 5). Excision with skin grafts was advised.

Operations were done at the Baker Memorial Hospital on June 21 and July 5, 1934. The areas of dermatitis over both knees were excised at the first operation. Thiersch grafts were applied to the granulating wounds at the second operation. Lesion over left elbow was excised and defect covered with full thickness graft. Recovery was uneventful.

Microscopical examination showed X-ray burns with one area of carcinoma over the left knee.

CASE 6. F. D., age 26, colored male, Massachusetts General Hospital 18136, was first seen on March 24, 1939. At 5 years of age he had received, in another hospital, x-ray treatment to his entire scalp for ringworm. The hair failed to grow on the right side. One year before entrance he noticed a small scaling area in the center of the bare area. This gradually increased in size. At times the crust came off, and there was profuse and persistent bleeding.

Examination showed an area of alopecia over the right temporoparietal region. In the center was a raised area 1½ by 1½ centimeters with moderate induration. There was loss of pigment in much of the area (Fig. 6). Malignancy in an irradiated area was suspected and excision was done of the portion showing the most marked changes. Microscopical examination showed deep fibrosis with a "verruca" in the center. The area was covered with a graft which was not entirely satisfactory, but healing eventually occurred.

CASE 7. I. H., age 50, was examined in July, 1934, complaining of ulcers on his legs. For many years he had suffered from eczema involving the whole body. He had tried every known remedy without relief. Seven years before he had received x-ray treatment to various parts of the body, but chiefly to his legs. Two years previously he began to develop an irradiation dermatitis on top of his eczema. One malignant ulcer had been excised.

Examination showed an extensive exfoliating eczema of the whole body. On the inner aspect of the right lower leg there was an area of skin with poor circulation. The skin was dry, showed numerous telangiectases, some heaping

up of the epithelium in the form of hyperkeratoses and numerous pinpoint ulcers. On the other leg there were numerous keratotic areas.

The first operation was done at the Phillips House on July 14, 1934. An area 3½ by 1½ inches wide was excised and a secondary graft done. Microscopical examination showed radiation dermatitis but no malignancy.

During the past 6 years numerous other areas on both legs, sometimes several square inches, have been excised and grafted. The circulation at the base of these ulcers has been very deficient and fat has been entirely absent. None of the specimens has shown malignancy. With the exception of a small malignant lesion on his nose he has not developed radiation dermatitis or necrosis anywhere except on the lower extremities. He is an extremely active individual on his feet. His dorsalis pedis arteries are palpable. Probably his activity has aided his circulation and has prevented extreme necrosis and gangrene of his extremities.

Group III. Roentgen therapy of lesions on the extremities. Case 7 cited above, could well be included also in this group. It is apparent from that case and those which follow that the same amount of therapy that would be used on the face, neck or trunk cannot be used safely on the extremities.

Case 8. M. S., Westfield Sanatorium 1145, age 65, was admitted on February 8, 1939, with a large ulcerated growth on the dorsum of the left wrist. The duration was 4 years and he had received no treatment. Examination showed an ulcerated lesion extending across the entire dorsum and lateral aspects of the wrist, measuring 9 by 7 centimeters. There was good motion of the fingers, but the wrist was fixed with 40 degrees dorsiflexion. The examining physicians stated that he would probably require amputation, but felt that roentgen therapy should be tried. Biopsy showed necrotic cancer.

During the next month he received 6000 r at 200 kilovolts through an 8 by 10 centimeter portal, directed to the dorsum of the hand, and 2100 r to the medial and lateral aspects of the hand, 400 r at a treatment. There was marked regression of the cancer but the ulcer became deeper, necrotic, and foul. Pain was not a great factor. Ten weeks later there was no healing, but no cancer could be seen (Fig. 7). Amputation was done at the junction of the upper and middle thirds of the forearm. The pathologist could find no cancer in the specimen submitted but there was marked irradiation reaction.

This is an example of roentgen therapy given to a region with poor blood supply and little subcutaneous fat in an elderly man. The dosage was adequate to destroy the cancer, but regeneration could not be expected to occur on a tendon sheath base, particularly in the face of extensive infection and necrosis. Amputation in such cases is the only satisfactory method of treatment.

Case 9. S. A., age 58, was first seen in 1924. She gave a story which dated back 29 years, having begun with a swollen gland in the neck which broke down and formed sinuses. She then had sinuses in the bones of her right wrist and jaw and later further sinuses over her ankles and bones of the lower leg. She was treated 20 years previous to examination by x-ray and again 13 years previously. She also had lupus on the face treated by x-ray. Apparently she had multiple manifestations of tuberculosis in the skin, bones, and glands.

At the time of the first examination she had extensive carcinoma on her nose. The entire nose was removed. Later she developed a carcinoma on the right side of the face in an area formerly treated by x-ray for lupus. The lesion on the right cheek was excised and closed with a large full-thickness graft. There was no recurrence of these areas after they were operated on. In 1935 she developed carcinoma of the left breast. Radical operation was done and the pathological report was colloid carcinoma without metastases. In 1937 she developed carcinoma of the right breast. Radical operation was done, and this was reported as grade 3 with axillary involvement. At this time she called my attention to a growth on the right leg in an area of x-ray dermatitis. This was excised and found to be carcinoma. Again in May, 1940, she appeared with another growth on the opposite leg. This was around a chronic sinus and this time the pathology was both tuberculosis in the sinus and carcinoma in the skin around it. At the present time she has metastases in her spine from the second carcinoma of the breast.

In this case her facial cancers occurred in old lupus scars. Even though she received roentgen therapy it is uncertain whether the therapy or the tuberculosis was the activating agent. It is striking that, next to her face the areas on the extremities should have been the first to break down.

Case 10. A. P., age 47, was admitted to the Pondville Hospital in May, 1938, with multiple basal cell carcinomas of the temple, back, and right ankle. Approximately the same dosage of roentgen therapy (high voltage) was given to each area and additional treatment a month later. All lesions healed and have remained healed until recently when the area above the right ankle became tender and broke down (Fig. 8). After 2 weeks he sought relief from his pain and the area was excised. Microscopical examination showed irradiation necrosis. This necrosis occurred 18 months after his last treatment.

Group IV. Injuries to roentgenologists and other workers in roentgenology.

Case 11. J. B., age 60, roentgenologist, was first seen in April, 1939 complaining of ulceration of the middle phalanx of the left index finger. For many years he had noted an increasing amount of dermatitis of his hands but the present lesion had come on rather suddenly. The left forefinger and middle finger showed very marked telangiectases particularly on the dorsum. The nail was corrugated and beneath it was a large area of hyperkeratosis. The nail was exceedingly tender. At the base of the nail, close to the inner phalangeal joint, was an area of ulceration (Fig. 9). The pain in this was severe enough to require opiates.

He was operated on at the Baker Memorial Hospital on May 2, 1939, and the involved area of skin on both the forefinger and middle finger was removed. The defects were covered with Thiersch grafts. The ulcer was found to extend deep down toward the joint and to have destroyed the tendon attached to the terminal phalanx. As a result, he had some permanent flexion of the terminal phalanx, and the tissues about the nail were extremely atrophied. Later amputation of the terminal phalanx was done on this hand.

The pathological report on area excised and on amputated phalanx was "irradiation necrosis with no malignancy."

Case 12. H. P., a 26 year old physician was examined on October 30, 1935. Fifteen months before he burned the fingers and thumbs of each hand while setting a fracture under the fluoroscope. It is said that this procedure re-

quired one and one-half hours. A marked reaction appeared within a week, followed by ulceration and severe pain in the right index finger. The ulcer was removed and a flap applied from the chest. Healing occurred in 6 months. He had previously developed a painful ulcer in the left index finger. Examination showed a gangrenous, acutely tender area covering the terminal phalanx and half of the middle phalanx of the left index finger. Partial amputation was advised and done by another surgeon. Six weeks later he again appeared with a new acutely painful ulcer at the tip of the middle finger on the left hand (Fig. 10). There was also an area of dermatitis and atrophy on the thumb. He was advised to enter the hospital the following day, which he did. In the interim the skin of the thumb broke down and a painful ulcer developed in a few hours.

Operation was done at the Baker Memorial Hospital on December 6, 1935. All the damaged skin on the left thumb and middle finger was excised and the defects closed with a full thickness skin graft. In February a new ulcer appeared on the right middle finger and the irradiated area was excised and grafted. All grafts took quite well and he has remained free from further trouble (Fig. 11, a and b).

CASE 13. E. F., age 70, former x-ray technician and photographer, was seen in August, 1937. He had done a great deal of work with x-ray during the early years of its development and had sustained extreme chronic burns of his hands. He had been treated at numerous hospitals and had many operations. On examination he showed loss of his forefinger and little finger on the right hand (Fig. 12, a). The ring finger was involved in a large, cauliflower mass which extended down into the palm. The function of the thumb and middle finger was fair. On the other hand he had lost two fingers. Operation was carried out at the Massachusetts General Hospital in August, 1939. The ring finger and corresponding metacarpal were removed together with the growth. A skin graft was applied over the defect (Fig. 12, b). There has been no recurrence. During the past year he has been able to do a good deal of careful work as a photographer and cabinet maker with a thumb and finger on one hand and a thumb and two fingers on the other.

Group V. Ulceration of an abdominal scar with fecal fistulas.

CASE 14. W. J., age 30, was first seen in 1921. A few months before he had noticed a mass in the left lower abdominal quadrant. He was traveling in Texas at the time and an exploratory laparotomy was done. A large retroperitoneal tumor was found and it was thought to be a sarcoma. No biopsy was done. A course of x-ray treatments was given following operation.

He came to Boston a few months later and had a second series of treatments. This time deep therapy was given at the Huntington Hospital through the anterior and posterior portals. Six months later he received further treatment through lateral portals. A few weeks later his abdominal wound broke open and he developed several fecal fistulas. He was operated on by the late Dr. R. B. Greenough and an anastomosis was done between the cecum and rectosigmoid. He continued draining through a fistula in the small intestine, however. A few months later he began to discharge large quantities of hair and a piece of jaw bone from his wound. This, of course, made the diagnosis one of dermoid cyst rather than one of malignancy. Gradually the entire abdominal wall broke down and he had numerous operations and closure of fistulas. Finally one small fistula remained together with the fistula into his dermoid cyst. About this time he developed pernicious anemia. As he happened to be under treatment at the Huntington Hospital at that time he came in charge of Dr. George Minot and his associates and he responded well to liver therapy. Due to the destruction of the abdominal wall and the abdominal muscles his abdomen was very much contracted and he walked in a bent over attitude and it was not possible for him to work. He gradually improved but in 1936 he developed metastatic carcinomas in the cervical lymph nodes. Later he was found to have a carcinoma of the posterior wall of the pharynx, and he died from this condition.

This patient was treated in the early days of deep therapy and while he did not have an amount that we would consider excessive today he did have more than his recently healed abdominal wound would stand. Infection from that ruptured wound destroyed much of the irradiated tissue over the rest of the abdomen.

Group VI. Necrosis of bone and cartilage.

CASE 15. J. K., age 63, was first seen at the Pondville Hospital on January 19, 1928, with an extensive carcinoma involving the left lower jaw and extending back to the anterior pillar and with induration extending into the submaxillary region. Roentgen examination showed bone destruction. The patient's mouth was fairly clean, and he was edentulous. Gold seeds of radon were inserted into the tumor and deep therapy was given externally. There was good response to the treatment. Three months later bare bone was visible, and he had a large opening in his cheek.

For the next 7 years the necrotic bone continued to come away. The bone was rongeured many times and numerous attempts were made to close the fistula. There was never any reappearance of the cancer. In May, 1935, the fistula was closed successfully and the last bit of exposed bone came away. He died without recurrence in 1938 at the age of 73 years.

Irradiated bone is "sick" bone, but it is not dead. There is no tendency to sequestration and there is no line of demarcation. We have successfully coagulated irradiated bone on several occasions and have produced heat necrosis with later sequestration.

CASE 16. A. B., age 59, was first seen in the cancer clinic of the Westfield Sanatorium on June 15, 1938, with a mixed basal and squamous carcinoma of the bridge of the nose, of 10 years' duration. He was given one treatment of high voltage therapy. The lesion had completely healed in 6 weeks, but there was edema and redness of the septum. Fourteen months later he complained of excruciating pain in his septum and shortly after a perforation appeared with relief of his pain. Thus definite destruction of cartilage occurred 16 months after therapy.

Group VII. Ligation of vessels supplying an irradiated area. In case of hemorrhage, ligation of the vessel supplying the part is often done. If this region has previously been subjected to roentgen damage, such a ligation may deprive the tissues of all their nourishment and gangrene may follow.

CASE 17. W. M., age 61, Pondville Hospital No. 4,391, was admitted on January 27, 1934, with an ulcerated, indurated lesion on the right side of his tongue. This was treated by electrosurgical excision and the implantation of

platinum needles. He later received irradiation to several hard lymph nodes in the right side of the neck.

One week after this treatment was completed he was readmitted because of severe hemorrhage from his tongue. The external carotid artery was ligated and the bleeding was checked. He was followed in the clinic. One month later a severe radiation reaction in the skin and mucous membrane of the mouth was noted. There was marked edema of the face and he was unable to open his mouth. Three weeks later he was again admitted.

He was in a critical condition. The edema of the face had increased. There was an area of gangrene of the entire field treated by x-ray. On removal of the gangrenous tissue extensive ulceration of the side of the tongue, the alveolus and floor of the mouth, was noted. Death followed in 5 days. No autopsy was performed.

CASE 18. A. C., age 50, was seen at the Massachusetts General Hospital in August, 1937 with a carcinoma of the buccal mucosa. He received high voltage therapy externally over a period of 1 month. After these treatments had been started he went to his dentist and had some teeth extracted. Two months later he had a severe hemorrhage from the cheek and had an emergency ligation of the external carotid artery. Within a few days there was evidence of circulatory change and he was referred to the Pondville Hospital December 20, 1937. There was marked edema with swelling of all the area which had been irradiated. Rapid changes occurred in the irradiated area and all the treated tissues became gangrenous and were removed. In spite of the large amount of therapy which he had received a recurrence developed along the jaw and extended to the tonsil. Death occurred within a few weeks.

Group VIII. Repeated roentgen therapy for plantar warts. We have recently seen a group of patients suffering from irradiation necrosis of the sole of the foot. In each case treatment had been given with relief at first. However, when treatment was given for a recurrence of the wart necrosis followed.

CASE 19. T. M., age 21, was seen on October 30, 1939. Four years previously he had received x-ray treatment for plantar warts. Several treatments were given at weekly intervals but the type of treatment and the dosage are not known. Three years later the warts recurred and he received treatment in November, 1938, February, 1939, and in May, 1939. High voltage therapy at a distance of 20 centimeters was used.

Fig. 1. Case 1. Irradiation dermatitis following roentgen treatment for superfluous hair. No malignancy.

Following treatment the warts cleared up and he spent his summer in active athletics, much of the time wearing sneakers. He knows of no direct trauma but in August a painful ulcer appeared and for 4 weeks he has been confined to a hospital and has required opiates to relieve his pain.

On November 4 he was operated on at the Baker Memorial Hospital. The lesion was excised down to normal fat. A pedicle graft was lifted from the opposite thigh and sutured in place on the foot. A plaster spica including both legs was applied and this was left in place for 2 weeks. At the end of this interval the flap was divided and sutured in place on the foot. Weight bearing was started 3 weeks later and he walked normally 2 months after removal of the ulcer. There has been no recurrence of the ulcer.

Fig. 2. Case 2. Irradiation dermatitis following roentgen therapy for superfluous hair. Carcinoma is present on the left side of face.

Fig. 3. Case 3. An area of irradiation dermatitis and probable carcinoma was excised 5 years before. End-result of Thiersch graft. Note the extreme whiteness of graft.

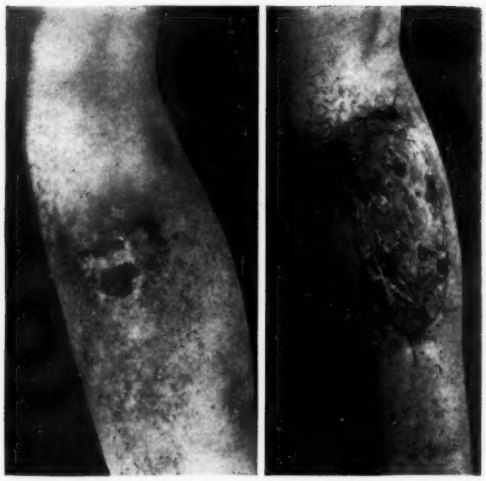

Fig. 4. Case 4. Left, irradiation necrosis after roentgen therapy for superfluous hair. Appearance of Thiersch grafts at first dressing after operation.

Group IX. Painful ulcers following successful eradication of cancer by roentgen therapy.

CASE 20. O. N., age 48, was seen in June, 1938, with a painful ulcer on the chest wall. Ten years before, the right breast had been removed for several solitary tumors. The pathologist reported that these were benign. However, 3 years later, a red nodule appeared in the scar. This gradually changed in size and appearance and 2 years ago she received x-ray treatments in a neighboring state. Following her treatment she developed a reaction which took 4 months to heal. It remained healed for 1 year and 8 months ago it began to break open. It has gradually spread until the entire irradiated area has become involved (Fig. 13, a).

Relief of pain was the problem in this case. It was not felt that the original lesion had been malignant and there

Fig. 5. Case 5. Irradiation necrosis after roentgen therapy for psoriasis. Carcinoma was present on the left.

Fig. 6. Case 6. Late irradiation necrosis after roentgen therapy for ringworm of the scalp.

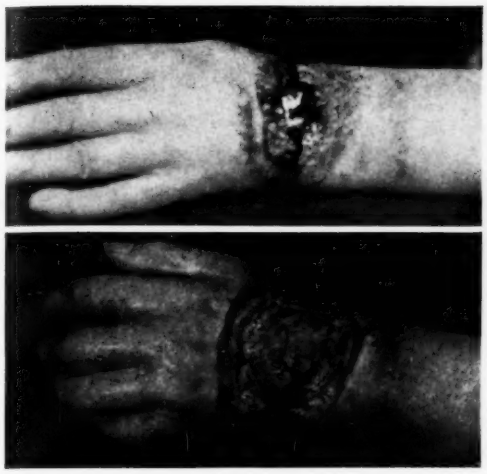

Fig. 7. Case 8. Above, carcinoma of dorsum of hand before treatment. Note that fingers are essentially normal. Below, after roentgen therapy. The carcinoma has been destroyed, but there is deep necrosis. Note the useless fingers. Amputation was done.

Fig. 8. Case 10. Late necrosis of skin above ankle 18 months after high voltage roentgen therapy.

had been no biopsy in the apparent recurrence. Complete x-ray examination of the bony skeleton was made and no metastases were found.

Operation was performed at the Baker Memorial Hospital on October 14, 1938. The entire area of dermatitis was excised down to the ribs and intercostal muscles. A flap 7 by 4 inches was dissected up from the abdominal wall and rotated to fill the greater part of the defect (Fig. 13, b). A second flap was dissected from the lower abdomen to fill the second defect. A small part of the flap sloughed and a skin graft was done 2 months later. The pathological findings were x-ray necrosis and inflammation but no tumor. She developed necrosis of one rib, and this gradually sequestrated. She had received complete relief from her chest pain and was able to be quite active again. However, about 6 months after the lesion was excised she began to show evidence of bone metastases. These developed rapidly and she died in September, 1939, with metastases in

Fig. 9. Case 11. Late irradiation changes in the fingers of a roentgenologist. Note the fissured nails, loss of pigment, the subungual hyperkeratosis and the ulcer at the base of the distal phalanx of the forefinger.

Fig. 10. Case 12. Partial amputation of left index finger after an acute x-ray burn. Note also ulcer of tip of middle finger and area of irradiation dermatitis on thumb.

Fig. 11. Case 12. a, Note amputated terminal phalanges of each forefinger and irradiation dermatitis of thumbs and middle fingers. b, After excision of areas of irradiation dermatitis and application of full thickness grafts. Note the poor result of treatment of the middle finger with its complete loss of fat and the prominence of the phalanx.

right humerus, right scapula, left femur and spine. She also developed extensive disease beneath pectoral muscles.

The ulceration in this case was caused by the legitimate attempt at destruction of her tumor. This was accomplished. Surgical treatment was attempted with the hope of permanent cure but proved to be only palliative treatment, because of the development of extensive metastases.

CASE 21. J. K., Westfield Sanatorium No. 1,536, age 58, admitted June 7, 1939, with a raised, ulcerated lesion 4 by 5 centimeters over the sternum. This had been present for about 20 years and a biopsy examination showed basal cell carcinoma. Definite fixation to the sternum made it appear inoperable. However, roentgenograms did not show invasion of the sternum (Fig. 14, a).

He was given 5600 r with the 200 kilovolt machine delivered through a 5.3 centimeter cone over a period of 17 days, ending July 8, 1939. There was immediate regression of the tumor. There was no sign of healing. Bone necrosis followed and deep infection of the chest wall required drainage. A large piece of sternum has come away but there is still a large area of radiation osteitis (Fig. 14, b).

The writer was asked to operate on this patient, but felt that roentgen therapy was better. Looking back, we now feel that excision with coagulation of the involved periosteum would have been a better method of treatment.

Group X. Roentgen therapy to lumbosacral region. During the past 2 years we have followed

Fig. 12. Case 13. a, Late results of roentgen damage to an early worker with development of cancer in damaged areas. Note the absence of two fingers. b, right, 16 months after excision of the cancer and application of a Thiersch graft, finger and thumb are very useful. Numerous areas of hyperkeratosis on the finger and thumb.

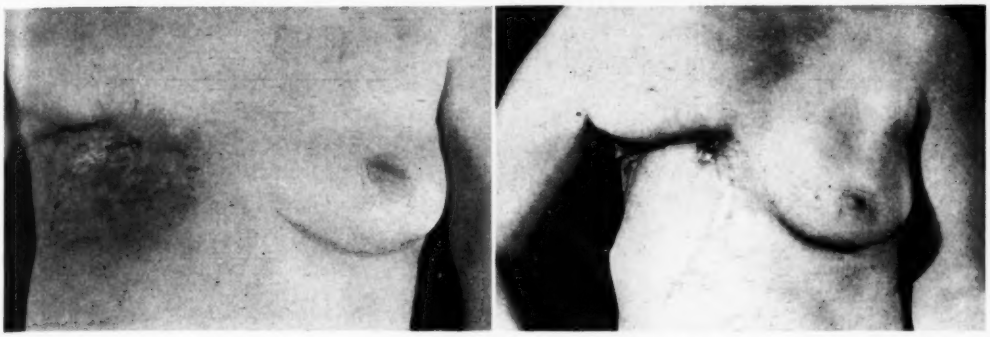

Fig. 13. Case 20. a, left, Recurrent carcinoma of breast following extensive roentgen therapy. The entire irradiated area is ulcerated and very painful. b, The ulcer has been excised and closed by means of a flap from the abdomen. A necrotic rib is shown. Patient has been relieved of all her pain.

4 patients who have developed radiation necrosis of the lumbosacral region. This appears to be a site particularly likely to be damaged by large doses of roentgen therapy. In the following case radiation necrosis occurred in this region and also on the anterior abdominal wall.

CASE 22. F. S., age 59, a retired school teacher, was seen in November, 1938, and admitted to the Baker Memorial Hospital. A tumor of the intestines had been removed in 1926, but no microscopic examination was made. In 1930 a second operation revealed "a very extensive carcinomatous involvement of all the retroperitoneal glands and liver" but nothing was removed for examination.

From 1930 to 1932 she received x-ray therapy (type and amount unknown) through anterior and posterior portals. In 1934 she developed induration about the umbilicus. This was excised but the wound never healed. Later she developed an ulceration over the sacrum. In the meantime she had noticed enlarged axillary and cervical nodes and as these responded to small doses of x-ray it was thought probable that these nodes as well as the abdominal nodes represented lymphoma. The ulcer of the abdominal wall had been present for 4 years and had troubled her chiefly because of the odor. The posterior ulcer, present for 3 years, gave constant pain.

Examination showed absence of the umbilicus. Surrounding its normal position was an extensive area of irradiation dermatitis with telangiectases around the periphery and a deep ulcer extending down to the fascia (Fig. 15, a). There was a similar ulcer with less depth over the upper portion of the sacrum (Fig. 15, b). Operation was advised.

On December 6, 1938, operation was performed on the posterior ulcer. An incision was made around the periphery of the irradiated tissue through normal skin. The wound edges were beveled in to the edge of the normal fat which

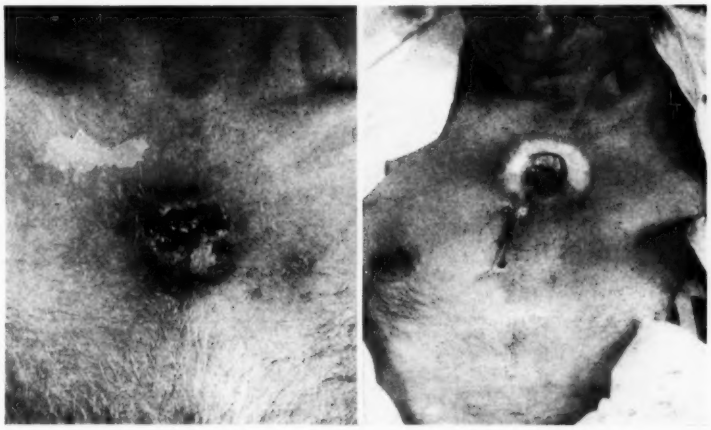

Fig. 14. Case 21. a, left, Basal cell carcinoma overlying sternum. b, The same lesion following deep therapy. The sternum is necrotic. An abscess around the lesion has been drained on the right.

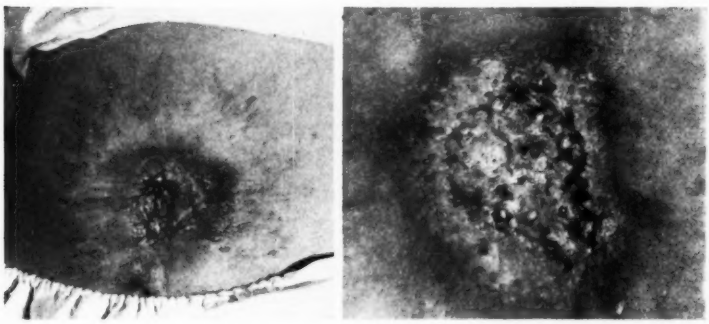

Fig. 15. Case 22. a, left, Irradiation dermatitis and necrosis of anterior abdominal wall about umbilicus. The necrosis extended to the peritoneum. Lesion excised and closed by flap from below. b, Same patient, showing similar area over sacrum. Lesion excised and closed by flaps from buttocks.

was entirely absent around the ulcer. One layer of fascia was removed. This left a layer of fascia overlying the muscles. Numerous incisions were made in this fascia to aid the formation of granulations. The fascia had a peculiar gray appearance and did not look healthy.

Two months later there was very little evidence of healing. The wound was covered with a gray hyaline-like scum which could be separated with scissors but which reappeared in 2 or 3 days. At the time of operation on the anterior wound this surface was again curetted and another layer of necrotic fascia removed down to the sacrospinalis group of muscles. Dakin's solution was found to be the best material to clean up the wound. On March 4 there still was little evidence of healing. The gray film (in some places 1 cm. thick) had reappeared. Again this was removed down to bleeding muscle and the entire area was covered with thick split grafts. Again the wound covered over with the gray slough and the grafts were apparently lost: Five weeks later a more radical method of closure was adopted. A large flap of skin and fat, measuring 7 by 4 inches, was removed from the right buttock and swung at right angles to cover the defect. The surface exudate was again curetted and to our surprise practically all of the skin grafts were present under this hyalinized layer. The grafts were removed and the graft sutured in place. As a result of this operation, one-half the wound was closed, for part of the graft sloughed and the rest pulled away. At this time it was noted that three spinous processes were exposed along the edge of the flap which stuck down to the muscle readily.

She was allowed to return home for a few months and then reentered the hospital. A large flap was dissected up from the left buttock, the irradiation scum and the exposed bone were removed and the flap was sutured in place. This procedure was satisfactory and the wound healed 14 months after the first excision.

During this same period the anterior abdominal wall ulcer was excised and closed by a right angle flap at one

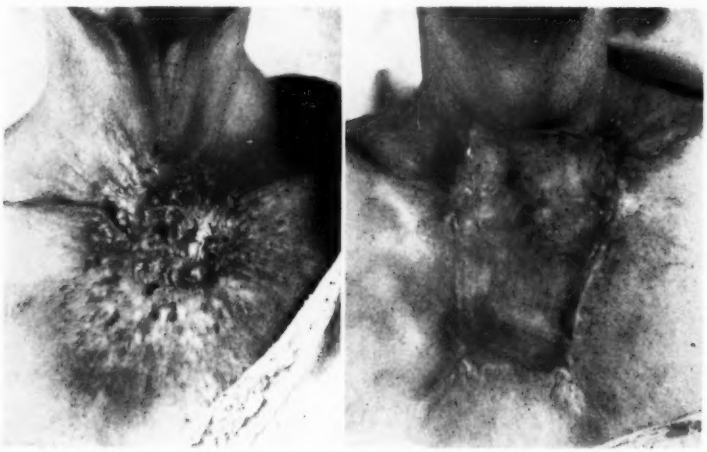

Fig. 16. Case 23. a, left, Irradiation carcinoma following low voltage roentgen therapy for hyperthyroidism. b, Same after excision and closure by Thiersch grafts.

sitting. The necrosis was found to involve all layers of the abdominal wall including the peritoneum, which had the typical gray exudate. Very little difficulty was experienced in the healing of this wound.

Group XI. Irradiation carcinoma following roentgen therapy for hyperthyroidism.

CASE 23. G. F., age 65, was admitted to the Phillips House on June 8, 1934 with an extensive ulceration over her neck and sternum. Twenty years before she had an enlargement of the thyroid, apparently toxic in nature. She received roentgen therapy in Tennessee, and the tumor decreased in size. The treatments were continued for 18 months and she then developed a "burn" which never healed. For the past 2 years nodules had been appearing in the ulcer.

Examination showed an extensive area of irradiation dermatitis extending from the thyroid cartilage down over the sternum to a point midway between the breasts and about 4 inches wide. The central half was ulcerated and nodular. There were no palpable lymph nodes (Fig. 16).

Operation was done on June 8, 1934. All involved tissues were excised and the wound was left to granulate. At no point did the growth perforate the fascia. Three weeks later Thiersch grafts were applied and healing was uneventful (Fig. 16 b). Microscopical examination showed epidermoid carcinoma, group 2. There was a wide margin of uninvolved tissue at the base of the specimen. Tumor cells invaded the subcutaneous fat. The muscle fibers showed degeneration. This patient has not been followed since operation.

Group XII. Complications from irradiation of carcinoma of the cervix.

CASE 24. M. L., age 53, was examined at her home June 28, 1938, suffering from cancer of the cervix. A course of roentgen therapy followed by radium was outlined. As she lived near the Pondville cancer hospital she asked that she might have her roentgen therapy as an outpatient. This was agreed to provided she enter the hospital for cystoscopy and intravenous pyelogram before starting therapy. This was done and no abnormality found in the urinary tract. For 10 days she returned for roentgen therapy each day. On the tenth day she complained of pain in the region of her right kidney. An intravenous pyelogram showed marked dilatation of the ureter and kidney pelvis.

This rapid change in the picture was undoubtedly caused by edema of the ureterovesical orifice caused both by the roentgen therapy and the disease process. A ureteral catheter was passed and the treatment was completed with the patient staying in the hospital. Had the condition not been detected early permanent damage to the kidney would have resulted.

CASE 25. F. H., age 59, was admitted to the Pondville Hospital on December 15, 1934. Examination showed a carcinoma which involved the entire cervix and extended onto the anterior vaginal wall. There was no infiltration of the broad ligaments. She was given a course of roentgen treatments to the pelvis, followed by two intra-uterine radium treatments 5 days apart. She then received a course of roentgen treatments to the perineum.

Six months later she returned, complaining of pain in the rectum and bleeding. An annular, constricting lesion was felt a short distance from the anus with a thick scarred area on the anterior wall. Biopsy showed radiation reaction with scattered cancer cells. No further treatment was given. During the next year she had a decreasing amount of discomfort in the rectum and was comfortable if she took oil. A note was then made that she had a stricture high up which admitted one finger. A year later she showed increasing signs of obstruction. A proctoscope could be passed without difficulty. The rectal mucosa was pale but not ulcerated. She complained of pain around the anus. An alcohol injection into the lumbar subarachnoid space gave slight relief for a time. Two years later an ulceration appeared on the anterior rectal wall below the level of the cervix. Biopsy was negative for carcinoma. The amount of pain increased and a second spinal alcohol injection was done without relief. She lost control of the sphincter entirely after this procedure.

Finally, on October 5, 1940 a colostomy was done. Exploration of the pelvis showed no recurrence of the cancer in the pelvis or in the large bowel. She has obtained relief from her pain.

This patient showed a stricture of the rectum and probably metastatic cancer of the cervix in the rectum 6 months after roentgen and radium treatment. The stricture persisted and an ulceration appeared 5 years after treatment. The satisfactory feature in this case is the apparent cure of the cancer of the cervix and the metastatic area in the rectum.

SUMMARY

Damage to tissues following irradiation may be due to faulty technique, improper dosage or screening, excessive doses particularly for benign lesions, heavy doses in the successful attack on a malignant growth, or to scattering or penetrating radiation of normal tissues around a malignant growth.

When the circulation of a region is poor, the damaging effect from irradiation is greater. After therapy the circulation becomes poorer in the treated area and any ligation of vessels to that region will result in gangrene of the area. Infection in a treated area may hasten necrosis. The extremities often have deficient circulation and they do not tolerate heavy doses well.

Cancer may develop in an area of irradiation dermatitis after a latent period of as short as 2½ years.

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THE PRESENT STATUS OF TREATMENT OF GYNECOLOGICAL CANCER

With Special Reference to Results Obtained Since Introduction of Supervoltage Roentgen Therapy—Statistical Analysis of Results from 1922-1935

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CARCINOMA of the female genital tract is more accessible to diagnosis and biopsy than carcinoma of many other organs. Carcinoma of the external genitals is always possible of free inspection and palpation, and biopsy is a very minor procedure. Cancer of the cervix likewise is possible of easy palpation and inspection with biopsy an equally minor procedure. Cancer of the uterine fundus, while not always palpable and not possible of inspection, is easily diagnosed by biopsy. Likewise malignant disease of the adnexa can at least be palpated. With these facts established it would seem that early diagnosis should be possible in all gynecological carcinoma. The fact that early diagnoses are not the rule is an evidence that many factors yet need emphasis and that education is still far from being complete.

Statistics from all clinics show that results from treatment of all kinds of gynecological malignancy are still far from what is desired. Also all clinics report that better results are obtained whenever the diagnosis is made early. The discouraging fact is that in so many cases when the patient first applies for treatment the lesion is already far advanced. We can only emphasize that education of both the profession and laity must be persistently continued. Thus far the educational program has not yielded this hoped-for improvement. The laity must still be informed as to danger signs, and the habit of frequent check-up examinations must become much more general. The profession must be spurred on to be more alert and methods of examination must become most painstaking.

It has been asserted by some workers (Schiller) that early superficial lesions in the cervix may exist a relatively long time before infiltration into the deeper tissues takes place. By taking advantage of the changed iodine reactions of the lessened glycogen content in malignant tissue, Schiller believes he can demonstrate suspicious areas before deep infiltration occurs. Although Schiller reports a good number of early carcinomas thus discovered gynecologists in general have not accepted the idea wholeheartedly. No less an authority than Novak intimates that after testing out the method he uses it less and less in his practice. It is doubtless true that the transition from normal to malignant tissue is not a sudden occurrence, and it probably covers a considerable period of time. The medical profession must use all aids in the diagnosis of carcinoma at this early stage. This will require the development of great clinical judgment as well as careful and frequent examination.

Gynecologists are continually confronted by the problem as to whether carcinoma of the cervix can be prevented by treatment of cervical lesions. This question can not be answered with much positiveness since authorities disagree on the relationship of cervical lesions to subsequent carcinoma. One school believes some constitutional factor, perhaps hormone influence, may be the underlying factor in the development of a carcinoma. It is also suggested by some that the usual cervical lesions considered precancerous by some may be due to an endocrine factor. Other authorities are quite positive that cervical lesions may be forerunners of malignant disease. Significant indeed are the series of cases reported showing the paucity of carcinoma after adequate treatment of cervical lesions. Also significant is the apparent fact that in series of cases developing carcinoma of the cervix, very few have had any treatment of cervical conditions. Surgical repair, amputation, cauterization, and conization would be considered as constituting adequate treatment. Until we have better evidence of the futility of such treatment it would seem wise to treat patients prophylactically along such lines.

From Harper Hospital.

Presented in the Cancer Symposium before the Clinical Congress of the American College of Surgeons, Chicago, October 21–25, 1940.

In speaking of prophylaxis we refer as a rule chiefly to cervical carcinoma. A possible relationship between a hyperplastic endometrium and a carcinoma of the endometrium has been suggested, but we know of no adequate prophylactic treatment.

In general, education and publicity should be directed toward urging patients to seek earlier treatment and to acquaint the medical profession with the methods of detecting lesions as early as possible.

About one-fourth of all cancers occurring in the female are in connection with the gynecological organs. Because of this high incidence and especially because of the diverse structural composition of the organs involved, no malignant neoplasms in any other location of the body create problems so important of interpretation and at the same time so difficult of solution.

From the therapeutic standpoint, the uninterrupted co-operation of the gynecologist and the radiologist over a long time is necessary to bring about the maximum of achievement. Changes inherent on the improvement of surgical technique are apt to influence radiation procedures; on the other hand, variations in the method of irradiation due chiefly to the continuous development of increasingly more powerful roentgen apparatus cannot remain without effect on surgical considerations.

It is the purpose of this paper to review the cases of patients treated at Harper Hospital from 1922 to 1935 inclusive and to discuss, on the basis of 5 and 10 year survival curves and other statistical figures the more salient points which have left their landmarks on the routine clinical procedures, thus leading to the present day status in the treatment of gynecological cancer. In 1932, a supervoltage roentgen therapy apparatus operating at a voltage as high as 750 kilovolt constant was installed in our institution and since 1933 patients with gynecological cancer have been irradiated with 500–600 kilovolt constant more or less routinely, so that an evaluation of the influence of this change on the 5 year results is also possible for a period of nearly 3 years (1933–1935 inclusive).

The attempt actually to cure carcinoma is of comparatively recent development. While various caustics and cauterizations have been used from time immemorial, the effort to eradicate a malignant disease has been attempted only since the development of surgery. For each type of cancer an operation has been developed. There is no doubt that the lack of any other possible method of cure gave this stimulus to the surgeon to tackle this problem, and even after the discovery of radium the development of the surgical treatment continued mostly when radium was not available. There is no doubt that the availability or non-availability of radium or x-ray was an influence that affected the plan of treatment. The earlier radical operations for carcinoma of the cervix were developed when radium was unknown or not available. As radium became better known, surgical operations for cervical carcinoma gradually went into the discard. There is now sufficient collected evidence to warrant the statement that the greatest advance in treatment of cervical carcinoma was made when the gynecologist relinquished the surgical treatment for radiation therapy. It is now no longer a question of competition between surgery and radiation, but rather a co-operation. In certain types of carcinoma this co-operation is well shown by the fact that both are employed, especially in carcinoma of the uterine fundus, ovarian carcinoma, and in carcinoma of the external genitals.

MATERIAL

The study is based on 845 cases of gynecological cancer of which 636 cases represent carcinoma of the cervix uteri, 77 carcinoma of the fundus uteri, 171 carcinoma of the ovary, and 31 carcinoma of the external genitalia. The cases were all followed up systematically year by year. In tabulating the 5 and 10 year results, attention was paid only to the "survivals." All patients who died from other causes than cancer were assumed to have died from cancer and about 2 per cent of the cases, being untraced, were likewise included among the dead from cancer. Thus the survival curves represent the lowest possible figures and their slight improvement may in time be expected, especially since experience shows that due to the extensive use of the indirect follow-up through the vital statistics bureau, most of the untraced patients are eventually found to be alive. Furthermore, all of the figures included herein represent absolute values. Not one single case was omitted from the compilation of the final results regardless of whether the originally outlined treatment was successfully brought to a conclusion or remained incomplete, and irrespective of whether a patient represented a fair possibility of cure from the beginning or already was in such an advanced stage that palliation could be expected at the best. If only the relative values are considered, making use of well selected groups of cases which are treated according to a program outlined in advance, then, of course, the survival curves assume somewhat higher values.

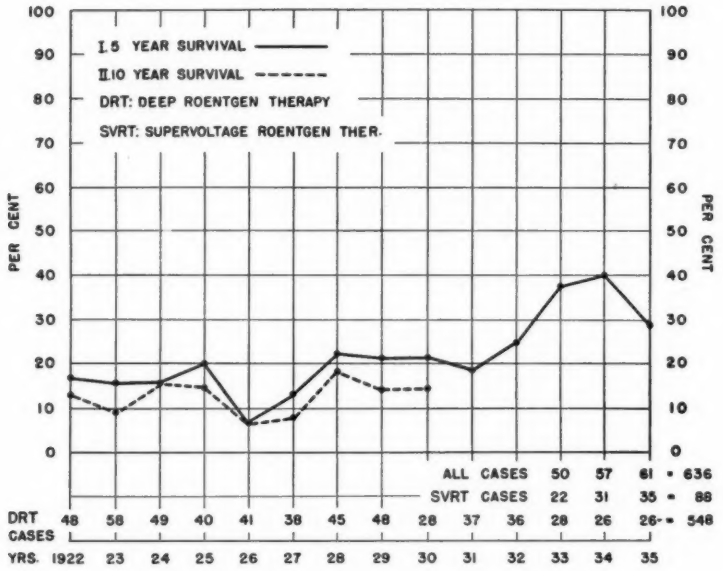

Fig. 1. Survival curves in carcinoma of cervix uteri.

METHOD OF TREATMENT

In the main, an association of surgery and irradiation was used freely, and, in preference to either method alone, whenever this was thought desirable.

The surgical technique in this series of cases has varied greatly. In the earlier cases of carcinoma of the cervix we find that panhysterectomy, both abdominal and vaginal, as well as the so called Wertheim operation, was occasionally performed. In conjunction with these surgical procedures deep roentgen therapy was always administered. Because of the rarity of early diagnosed cases these operations were of unusual incidence rather than the rule. Because of the apparent favorable results retained from radium in some of the advanced cases, the use of this agent gradually replaced surgical operations even in early cases, and it has now been several years since surgical cure of any kind has been attempted.

For carcinoma of the uterine fundus the earlier cases were considered adequately treated when a wide panhysterectomy was performed. Later experience has shown, however, that while this may effect a cure in the lower grades of malignancy, it is not adequate for the higher grades of malignancy. Therefore, in the later cases of carcinoma of the uterine fundus, all patients have been treated by both surgery and radiation.

During the course of time all surgical procedures, because of the addition of radiation therapy, were reduced to more conservative interventions.

The technique of irradiation consisted in the combination of intracavitary radium and external roentgen therapy whenever possible. From 1922 to 1928, the radium dose varied from 1200 to 2400 milligram hours for a single and from 3600 to 5000 milligram hours for a total application. Since 1928, it has been increased to from 3600 to 5000 milligram hours for a single and from 7200 to 10,000 milligram hours for a total application, this change accounting for some improvement in the survival curves, especially as shown in connection with the carcinoma of the cervix. The roentgen therapy was carried out with such an exposure as to obtain the maximum tolerable biological reaction. Apart from minor details, the method of procedure remained essentially the same, but the quality of the rays was changed in 1933. Thus from 1922 to 1932, inclusive, the so called deep roentgen therapy with 200 kilovolts (1 millimeter copper forefilter) was used and since 1933, supervoltage roentgen therapy with 500 to 600 kilovolts (7 millimeters copper forefilter) has been substituted for most of the cases of gynecological cancer. The effect of this change is evidenced on the survival curves of each type of gynecological cancer as discussed below.

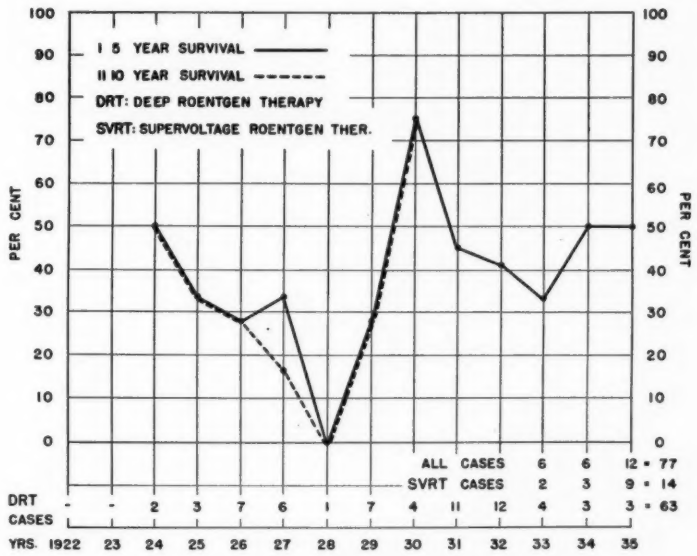
I 5 YEAR SURVIVAL
II 10 YEAR SURVIVAL
DRT: DEEP ROENTGEN THERAPY
SVRT: SUPERVOLTAGE ROENTGEN THER.
PER CENT
ALL CASES 6 6 12 = 77
SVRT CASES 2 3 9 = 14
DRT CASES - - 2 3 7 6 1 7 4 11 12 4 3 3 = 63
YRS. 1922 23 24 25 26 27 28 29 30 31 32 33 34 35

Fig. 2. Survival curves in carcinoma of fundus uteri.

1. Carcinoma of cervix uteri. In this group, in the first years as mentioned before, an operation was performed in the early cases and roentgen therapy was used prophylactically, whereas the more advanced cases were treated by a combination of intracavitary radium and external roentgen therapy. During later years, practically all of the cases were subjected to irradiation, and operation was performed only in rare instances. Prior to 1928, the dosage was distributed rather equally between the radium and roentgen rays, but since that year, the intracavitary application of radium has been made the main method, the largest tolerable dose being administered. The roentgen therapy thus became of secondary importance, its aim being merely to make up the deficient dose from the radium around the periphery of the pelvis especially in the regions of the distant parametria. This aim was facilitated since 1933 by the introduction of the more penetrating rays of supervoltage roentgen therapy.

As shown in Figure 1, the 5 and 10 year survivals between 1922 and 1928 averaged 16 and 12 per cent, respectively; from 1928 to 1932, they were raised to 21 and 15 per cent, respectively; and since 1933, the 5 year survivals have reached the average of 35 per cent.

2. Carcinoma of fundus uteri. In this group, a combination of surgery and radiation therapy was used whenever possible throughout the entire period. The procedure, as far as the irradiation is concerned, has moved along the same lines as employed in carcinoma of the cervix uteri, and the results are evidenced in the survival curve as shown in Figure 2. As is seen, the average of five year survival has been raised from about 30 per cent prior to 1930 to 45 per cent after that year and to nearly 50 per cent after 1933. The 10 year results here run a rather close parallel to the 5 year results. As already stated, however, these figures represent absolute values and therefore all cases which from the beginning have proved inoperable are included.

In considering separately the operable cases, that is, the group in which a combination of surgery and radiation therapy was used, a sharp line must be drawn between two distinct procedures.

TABLE I.—CARCINOMA OF FUNDUS UTERI
FIVE YEAR SURVIVALS

Method of treatment	Cases treated	Cases well	Percentage
Hysterectomy — postoperative irradiation	36	20	55
Pre-operative irradiation + hysterectomy 6 weeks later + postoperative irradiation.	7	5	71
Total operable cases	43	25	58
Radiation therapy alone in inoperable cases	34	10	29
Total of all cases	77	35	45

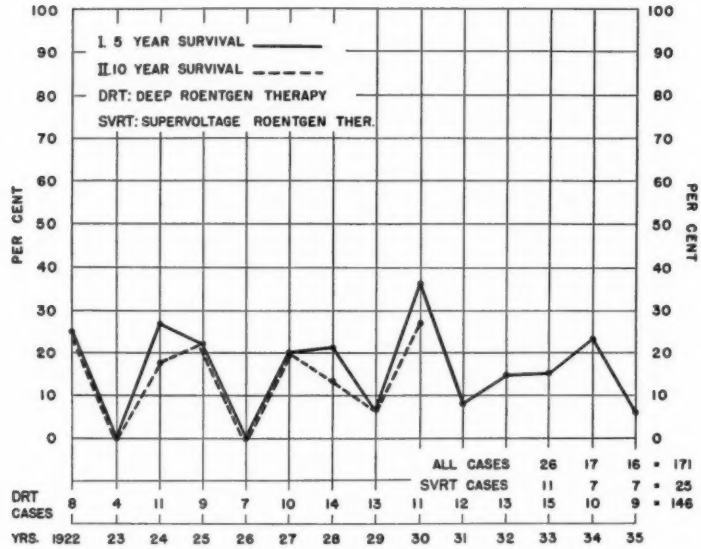

Fig. 3. Survival curves in carcinoma of ovary.

In one, the operation, consisting mostly of panhysterectomy, was performed as soon as the diagnosis was established and the radiation therapy was administered after operation. In the other, a full course of intracavitary radium and external roentgen therapy was given first and the operation performed after the subsidence of the biological effect from the irradiation, usually 6 weeks later. Further irradiation, consisting of roentgen therapy alone, was then given in the postoperative period. The results obtained by these procedures are illustrated in Table 1. As is seen, whereas a 5 year survival of 55 per cent was obtained in the first, this rose to 71 per cent in the second, the total figure for all operable cases representing 58 per cent.

3. Carcinoma of ovary. Although the malignant neoplasms pertaining to the ovary may show pathologically diversified appearances, from a clinical standpoint it seems practical to include them under one heading. In most cases, a combination of surgery and radiation therapy was necessary at one time or another. The predominating principle throughout the entire period was that whenever a patient constituted a good operative risk, the large neoplastic masses were removed by surgery and then irradiation was instituted. In other instances, radiation therapy was given in a preliminary way and the operation reserved for the period when the biological reaction from the irradiation had cleared up. In still other instances, both the operative procedure and the irradiation were repeated or even alternated many times for several years, depending on the clinical course.

As shown in Figure 3, the 5 and 10 year survivals represented broadly 20 and 18 per cent, respectively, throughout the entire period. Curiously enough, the addition of supervoltage roentgen therapy in the group treated so far, contrary to expectations, did not seem to have influenced the survival curves. The reason for this is not quite clear and it is possible that with a larger number of cases, the situation might be changed considerably.

4. Carcinoma of external genitalia. Of a total of 31 cases of carcinoma of the external genitalia, 14 occurred on the labia, 10 in the vulva, and 7 within the vaginal canal. A combination of surgery and radiation therapy was used in most cases, the technique of procedure being greatly individualized. In carcinoma of the labia and especially of the vaginal canal, at times it was found necessary to rely on the radiation therapy alone. As shown in Table II, the 5 year survivals amounted to 29 per cent for the labia, 10 per cent for the vulva, and none for the vagina. The number of cases treated with supervoltage roentgen therapy is as yet too small to permit an estimation of the value of this method.

ANALYSIS OF STUDY

In reviewing the results of the above groups several facts become of special interest. The most important, perhaps, among them is that the addition of radiation therapy has greatly changed the conception toward surgical approach. In many instances, operation has become less radical, in others it has been omitted altogether or made an integral part of radiation therapy and again in others the time of intervention has been readjusted so as to utilize the biological effect of the irradiation to the best advantage. In carcinoma of the cervix uteri, for example, surgery is now almost never a factor in curative treatment. In carcinoma of the fundus uteri, surgery continues to play the predominant rôle, but is best performed, after the administration of a full course of radiation therapy as soon as the biological reaction has subsided. There are two reasons why such a procedure is more advantageous. First, the intracavitary application of radium in combination with external roentgen therapy permits a more homogeneous irradiation of the entire pelvis, whereas if the uterus has been removed, the intra-uterine and intracervical insertion of radium, of course, becomes impossible and thus the radiation is, of necessity, less thorough. Second, experimental evidence of Drs. Altemeier and Jones shows that if an operation is performed within 4 to 6 weeks of the irradiation of the peritoneum, there is considerably less danger of infection and thus the postoperative mortality is greatly reduced. It must be mentioned, however, that if the irradiation has been repeated for several series, or given in such a way as to produce considerable fibrosis of the normal structures, then the subsequent operation may become very difficult. In carcinoma of the ovary, surgery may precede radiation therapy or may be undertaken at any time during the course of irradiation. In carcinoma of the external genitalia, the time of intervention and the indications for the two procedures are individualized from case to case. In discussing the surgical aspect perhaps one may also state that because of the not altogether negligible incidence of primary carcinoma in cervical stumps and because of the great limitations in appropriately treating such lesions, the removal of the entire vaginal portion of the cervix may appear advisable whenever a hysterectomy is performed for any other reason. In this way, the removal of the cervix may constitute a prophylactic measure.

Another fact is that irradiation, whenever possible, must be carried out by using a combination of intracavitary radium and external roentgen therapy. When the radium is applied, the prime consideration is given to this agent and the dosage is outlined in such a way as to permit its maximum use compatible with the tolerance of the surrounding normal structures. However, since radium alone, unless greatly overdosed, fails to reach the distant portions of the parametrium, it is necessary to make up this deficiency in dosage by the addition of external roentgen exposure. In the cases in which the radium cannot be applied, roentgen therapy becomes the sole method of procedure and hence its dosage must be increased and so adjusted as to meet the diversity of the problems created by the variation in the clinical extent of the malignant process.

TABLE II.—CARCINOMA OF EXTERNAL GENITALIA—FIVE YEAR SURVIVALS

Organ	Cases treated	Cases well	Percentage
Labia	14	4	29
Vulva	10	1	10
Vagina	7	..	..
Total	31	5	16

A third fact is that supervoltage roentgen therapy seems to acquire an increasing value in the treatment of gynecological cancers. There are at least three reasons, from a physical standpoint, why supervoltage roentgen therapy is considered superior to the deep roentgen therapy. First, there is a greater differential action of the radiation with increasing voltages, permitting the administration of a proportionately larger total dose; second, there is an increase in the total energy which can be delivered to obtain the same skin erythema; and third, there is an increase in the depth dose making a larger absorption at the site of deep seated lesions possible. Clinically this means that a larger total dose can be administered to the carcinoma with lesser injury to the skin and the surrounding structures. The technical procedure becomes simplified and at the same time the homogeneity of the irradiation is increased. The definite curative value of the method, however, will depend very much on the malignancy index of the neoplasm to be irradiated. Only in those instances in which the neoplasm remains of local character for a longer while may one expect any advantage from improving the efficacy of the irradiation, whereas if the malignant process has already produced distant metastases, any form of therapy will remain futile. There is, perhaps, no other field in which these requirements are met as satisfactorily as in the gynecological cancers. Especially is this true of the carcinoma of the cervix uteri in which the neoplastic invasion remains localized in the pelvis for a relatively long time, the fatal complications usually arising from

secondary effects on the neighboring structures or organs (2). If a better distribution of the irradiation can cover the neoplastic area in a more homogeneous manner, the chances for an improved result over that obtained with deep roentgen therapy is evident. Indeed, a study of the survival curves seems to support such a view. Although the number of patients treated is not yet sufficiently large to warrant final conclusions, nevertheless it appears that the addition of supervoltage roentgen therapy since 1933 has resulted in some rise of the 5 year survival curves in most gynecological cancers.

SUMMARY AND CONCLUSIONS

A total of 845 cases of gynecological cancer treated at Harper Hospital during 1922–1935 inclusive was analyzed and the absolute 5 and 10 year survivals studied.

In the main a combination of surgery and radiation therapy was used whenever possible, excepting the carcinoma of the cervix uteri. Of the agents employed for the irradiation, the radium, in the form of intracavitary application with the largest possible doses, was always given prime consideration. The roentgen rays were relegated to the secondary rôle of making up the deficiency of dosage at various points, especially toward the periphery of the irradiated pelvis. The gradual replacement since 1933 of the deep roentgen therapy (200 kilovolt constant, 1 millimeter copper) with the supervoltage roentgen therapy (500 to 600 kilovolt constant, 7 millimeters copper) has not changed this conception. Only the cases not amenable to surgery and unsuitable for intracavitary radium were treated by roentgen therapy alone.

Attention may be called to the following facts for the individual groups:

1. In cancer of the cervix uteri, radiation therapy, with few exceptions, constitutes the method of preference. The increase of the radium dose to the maximum tolerable has raised the 5 and 10 year survivals from 16 and 12 per cent to 21 and 15 per cent, respectively, and the supplanting of deep roentgen therapy with supervoltage roentgen therapy has now brought up the 5 year survival to practically 35 per cent.

2. In carcinoma of the fundus uteri, and in those cases of carcinoma of the cervix uteri in which a hysterectomy is performed, the optimum time for the operation is within 6 to 10 weeks following the completion of a preliminary series of radiation therapy consisting of intracavitary radium and external roentgen therapy. Further roentgen therapy is given in the postoperative period. By thus proceeding, the 5 year survivals were increased to 71 per cent as compared to 55 per cent when the operation was done first. The absolute 5 year survival of all cases treated since the introduction of supervoltage roentgen therapy approaches 50 per cent.

3. In carcinoma of the ovary a combination or alternation of surgery and radium therapy is used freely. The 5 and 10 year survivals continued to move around 20 and 18 per cent, respectively, throughout the entire period. Contrary to expectation, supervoltage roentgen therapy has brought no improvement in the survival curve.

4. In carcinoma of the external genitalia, the indications for operation and radiation therapy are greatly individualized. In lesions around the vulva, operation becomes the major procedure, whereas for skin cancers of the labia and especially the carcinomas of the vaginal canal one may have to rely entirely on radiation therapy. The 5 year survivals for the entire group represent 16 per cent and the 10 year survivals run a close parallel.

All in all, it appears that notable progress has been made in the treatment of gynecological cancer. The absolute survival curves obtained so far, though not the apogees of achievement, represent results which can not but encourage us to further increase our efforts in combating this very malignant disease.

The co-operation of the Department of Roentgenology is hereby acknowledged. All radiation data and discussion has been graciously contributed by Dr. Trian Leucutia, Head of Roentgentherapy.

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FRACTURES AND OTHER TRAUMA

HOMOLATERAL DILATATION OF THE PUPIL, HOMOLATERAL PARESIS AND BILATERAL MUSCULAR RIGIDITY IN THE DIAGNOSIS OF EXTRADURAL HEMORRHAGE

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EXTRADURAL hemorrhage occurs in approximately 3 per cent of the total number of cases of acute head injury. Since the classical paper by Jacobson formulating the modern conception of the clinical syndrome, the diagnosis of extradural hemorrhage has rested in brief upon the sequence of an initial period of unconsciousness following trauma to the head, a lucid interval, the reappearance of loss of consciousness and contralateral paresis commencing in the face or in the upper extremity with or without localized convulsions. In spite of the apparent simplicity of the syndrome, the mortality from this lesion remains unduly high.

In a group of 177 cases collected from the literature during the past 18 years, the mortality attained a level of 56.5 per cent.[1] Even more striking are the statistics of Le Count and Apfelbach and of Vance. These observers studied a total of 1,016 cases of acute head injury at autopsy and in this number observed 165 cases of extradural hemorrhage, the clots from which were considered large enough by these observers to produce appreciable and presumably fatal compression of the brain. Kennedy and Wortis have stated, after a study of similar totals, that "There is a great discrepancy between the number of cases of epidural hemorrhage recognized clinically and the number remaining undiagnosed until they reach the postmortem table. In our opinion this is due to the fact that the syndrome of epidural hemorrhage is much too rigid."

This high mortality rate may be due in part to concomitant severe injury to cerebral tissue apart from the extradural hemorrhage. It may be due to the essentially acute character of the hemorrhage and the inability to secure prompt neurosurgical intervention. There remain, however, the indisputable facts emphasized by Kennedy and Wortis that uncomplicated extradural hemorrhage may not conform to the accepted clinical syndrome and that the nonrecognition of such aberrant forms constitutes an important factor in the continual elevation of mortality statistics.

In this paper, 3 selected cases of extradural hemorrhage are discussed as classical or aberrant forms of the same pathological entity and the disturbances responsible for the aberrant forms are pointed out.

CASE 1. M. C., aged 13 years, history no. 59,657. Classical form of extradural hemorrhage. History of initial trauma with immediate loss of consciousness for 15 minutes, 28 hours prior to admission. Lucid interval until 10 hours before admission, followed by the slow onset of restlessness, coma, weakness of left upper extremity, dilatation of right pupil, and convulsive movement of left face and left arm. Roentgenogram of the skull was negative for fracture. Right extradural hemorrhage. Operation. Recovery.

While riding a bicycle, patient collided with another cycle rider and fell to the ground, striking the right frontal region of the head with considerable force. A history was secured from the patient at a later date that he was stunned and not completely unconscious, but was cognizant of his surroundings although unable to move. Five minutes after the initial trauma, he was able to walk a number of blocks to his home. He was at once taken to the office of his family physician who sutured a laceration in the right supra-orbital region. He vomited once at this time but was able to walk home where he went to bed. He stated that he recalls nothing of his subsequent course one hour after going to bed. The patient remained restless throughout the night, vomiting frequently, and in the morning could be aroused with difficulty. Approximately 10 hours before admission, restlessness was superseded by an increasingly deeper coma. Convulsive movements were noted at this time about the left side of the face and 5 hours later progressed to involve the left arm and later the left leg.

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[1]See refs. 12, 17, 21, 28, 31, 32, 34, 40, 41.

The admission temperature was 37.6 degrees C.; pulse, 60; respirations, 24; and blood pressure 116/83. The patient was deeply comatose, reacting only to extreme pressure over the supra-orbital areas. His reaction to such painful stimuli elicited a conspicuous flaccid hemiparesis, involving the left facial musculature, and left arm and leg. There was an ecchymosis over the right temporal region and a sutured laceration in the right supra-orbital region. The right pupil was dilated and fixed; the deep tendon reflexes on the left side were subdued. Routine blood and urine studies were negative. Stereoscopic lateral and anteroposterior views of the skull were negative for any evidence of fracture. A diagnosis of an extradural hemorrhage was made, situated on the right side. The hemorrhage was exposed through a small decompression opening, a large extradural clot evacuated, and a laceration of the main trunk of the middle meningeal artery, 3 centimeters distal from the foramen spinosum, was controlled. Four hours following this procedure, the patient was alert and oriented. On the second postoperative day, the neurological examination was negative.

In a chronological consideration of the classical syndrome of extradural hemorrhage, the location of the initial trauma is of primary import. Such hemorrhage may occur from rupture of the middle meningeal artery, the accompanying veins, or one of the major venous sinuses, chiefly the longitudinal or sphenoparietal. Obviously, as pointed out by Mellinger and Rawling, bony injury localized to or involving secondarily the squamous portion of the temporal bone is more likely to produce a tear in the middle meningeal artery and associated venous structures. That such a lesion may develop without a bony injury has been pointed out early by Bell and later by Jacobson who presented 8 cases out of 70 without fractures of the skull, particularly noted in Cases 2, 3, and 59, and is further confirmed by the case just detailed. In many cases, in which a fracture of the skull is present, ecchymosis and edema in the temporal region arising from a linear fracture of the temporal bone correctly suggest the formation of an underlying extradural hemorrhage.

Jacobson particularly emphasized his observation that the lucid interval may show marked variations, and in his cases, the evidence of cerebral compression occurred from 15 minutes to 4 days after the initial trauma. The lucid interval may be completely absent as it was in 32 of 63 cases recorded by Jacobson in which particular attention had been directed toward this detail. Absence of the lucid interval indicates a severe and concomitant cerebral injury or a complicating factor such as alcoholism, and as Verbrugghen has noted recently, the diagnosis then must rest upon the presence of localizing signs or, as has been advised by Dandy and others, upon the use of diagnostic trephine. The length of the lucid interval in uncomplicated extradural hemorrhage in all probability rests upon the rapidity of the development of the hemorrhage. This in turn is a measure of the type of vascular lesion, be it artery, vein, or sinus, and the resistance to stripping of the dura from the bone (Dandy) or the extent of original shaking of the dura away from the bone (Bell). Characteristically as the lucid interval lapses, bradycardia will develop.

In the majority of cases the expanding clot forms in the temporal fossa adjacent to the vascular tear involving the meningeal artery or veins. In this location, and as it expands, the mass causes pressure upon the lateral aspect of the motor cortex causing first a contralateral facial paresis, progressing to involvement of the arm and lastly the leg. Progressive cortical irritation may likewise explain the progressive localized convulsive state. The presence of such a hemiparesis may be elicited in unconscious patients only by extraordinarily painful stimuli. Equally important variations of peripheral motor defect will be discussed in the second and third cases of this report. Confirmatory evidence of the presence of an extradural hemorrhage may be induced from roentgenographic evidence of a fracture line crossing the vascular channel of the middle meningeal artery and from manometric evidence of a high intracranial pressure. Blood in the spinal fluid may or may not be present, depending upon the presence or absence of associated cerebral injury.

CASE 2. M. W., aged 46 years, Lynchburg Hospital, Lynchburg, Virginia. Aberrant form of extradural hemorrhage. History of initial trauma with no lucid interval and persistent loss of consciousness. Laceration of right temporal and left frontal region. Cerebrospinal fluid draining from right ear. Onset of paresis involving face and arm, right, 6 hours after admission. Transient dilatation of right pupil. Left trephine and decompression. Right trephine and removal of extradural hemorrhage. Exitus and autopsy. Multiple fractures, base of skull. Subarachnoid hemorrhage. Extradural hemorrhage, operative defect, right. Herniation of hippocampal gyrus, bilateral.

A 46 year old white man was hospitalized 1 hour following an automobile accident with a history of complete loss of consciousness since the time of the initial trauma. Upon admission, he was semistuporous, responding only to painful and loud auditory stimuli. There were superficial lacerations in the right temporal and left frontal regions of the scalp. There was a bloody serous discharge from the right ear. On admission neurological findings were normal and remained so until 6 hours following admission when a flaccid paresis of the right upper extremity was noted. Fourteen hours after admission, the right sided weakness involved the face but at no time were convulsive movements seen. The patient was examined at this time in consultation by Dr. Harvey Brownley of Lynchburg, Virginia, who pointed out during the period of his examination a dilated pupil on the right, which reacted sluggishly to light stimulation. This transient dilatation of the right pupil persisted for 30 minutes, and following this time until the patient's death, both pupils remained in mid-position, were equal, and reacted normally. The patient's status did not change until 33 hours after admission when the state of

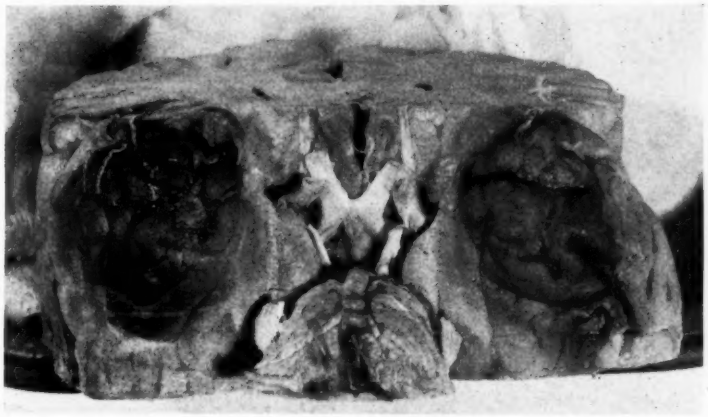

Fig. 1. Extradural hematoma, right. Bilateral herniation of hippocampal gyri, more marked on right. Case 2.

consciousness deepened to complete coma and the body temperature rose to 101 degrees F. A trephine and subtemporal decompression were done on the left side. The brain appeared grossly normal but under extreme tension. The patient's general condition improved until 22 hours later when a second break in compensation occurred, marked by a rise in temperature to 103 degrees, the onset of tachycardia, and renewed coma. In this period, there was no change in the neurological status. A trephine on the right side disclosed a large extradural hemorrhage which was removed through a small decompression opening. A rent in the anterior limb of the middle meningeal artery was noted as the probable focus of the hemorrhage. Temporary improvement was manifest following this procedure but exitus occurred 6 to 7 hours after the second operative procedure.

The postmortem examination was restricted to the contents of the cranial cavity. The extradural hemorrhage had been evacuated, but the brain had not filled out the remaining defect; the typical flat depression of the temporal lobe remained. The striking feature of the gross appearance of the brain was the marked herniation of both hippocampal gyri, particularly on the right (Fig. 1). Serial sections of the brain showed no obvious change from normal. Due to fixation, microscopic study could not be made. The base of the skull showed a bursting type of fracture with longitudinal involvement of both petrous pyramids, the cribriform plate, and the right occipital bone involving the foramen magnum. The meninges over the base of the brain were filled with bloody fluid.

Earlier recognition of this aberrant form of extradural hemorrhage was rendered difficult by the presence of homolateral hemiplegia and by the failure to interpret the significance of transient dilatation of the homolateral pupil. The significance of unilateral dilatation and fixation of the pupil in individuals with acute head injuries has been a matter of study since the early contributions by Macewen (26), Hutchinson, and Jacobson. The value of this sign in the presumptive diagnosis of a traumatic ipsilateral expanding intracranial lesion, extradural or subdural in location, has been abundantly confirmed by the clinical studies of Hoessly, Holman and Scott, and Kaplan, who have directed their studies from this particular point of view. Supportive evidence is present in a mass of papers discussing the subject from a more general point of view. Blakeslee has discussed 610 cases of skull fractures in which 378 manifested pupillary changes. Homolateral dilatation and fixation of the pupil was present in all cases of extradural hemorrhage in this series and frequently occurred in subdural hemorrhage. Wortis and Kennedy noted anisocoria in 220 of 1,000 cases of head injury. In 17 cases of extradural hemorrhage, the authors reported a dilated pupil on the homolateral side in 7, and on the contralateral side in 4. In 42 subdural hematomas, they described a dilated pupil on the homolateral side in 30.

Gurdjian discussed 16 cases of extradural hemorrhage, in 12 of which a dilated pupil was encountered on the homolateral side. McKenzie recorded 20 cases of extradural hemorrhages in which 15 had a homolateral dilated pupil. Jelsma reported 42 cases of subdural hematoma from the literature, in 36 per cent of which the ciliary part of the third nerve was affected. Munro, on the other hand, has stated (32, p. 147), "Fixed dilatation of one pupil, usually without demonstrable ptosis of the upper eyelid, occurs often. It is as common opposite the hematoma (subdural) as it is on the same side." On the other hand, in 48 cases of subdural hematoma, noteworthy for the low mortality rate of 4 per cent, Kunkel and Dan-

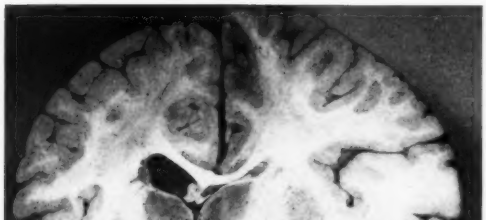

Fig. 2. Glioma of left temporal lobe. Herniation of hippocampal gyrus. Museum specimen, Duke Pathological Laboratory.

dy recorded anisocoria in but a single case. Pringle stated that a wide, nonreacting pupil is met on the same side as the hemorrhages in some cases. He felt that it was more important that a pupil, which is small when the patient is first seen, later becomes wide and nonreacting. Holman and Scott, and Cairns have emphasized the possible transient character of this pupillary reaction.

General agreement appears to exist concerning the significance of a unilateral dilated pupil in acute head injuries, as illustrated again in the first case recorded. That a transient dilatation may be of equally profound localizing import is pointed out by the clinical course of the second case. The mechanism responsible for this phenomenon in acute head injuries has been demonstrated but recently. Macewen (27), Cushing (7), Meyer, and Vincent, David and Thiebaut have demonstrated ipsilateral herniation of the hippocampus producing pressure upon the third nerve in cases of brain abscess and tumor together with resulting vascular phenomena due to obstruction of the posterior cerebral artery. The regional anatomy and clinical significance of the resulting tentorial pressure cone has been amply discussed and illustrated by Jefferson (18) in cases of brain tumor. Such a herniation in the presence of a temporal lobe tumor is demonstrated in a museum specimen in the Duke Pathological Laboratory, a dilated and fixed pupil being recorded in the clinical history, (Fig. 2). Hoessly stated from a study of his traumatic cases that bilateral dilatation of the pupil was due to a central destruction of the sympathetic supply with an accompanying release of the tone of the oculomotor nerve. He felt that unilateral dilatation of the pupil must be due to trauma upon the peripheral portion of the nerve. Blakeslee and Cairns stated that unilateral fixity and dilatation of the pupil commonly is caused by cortical injury. Kaplan, Gurdjian, and Holman and Scott have pointed out that the third nerve is peculiarly susceptible to pressure from above and laterally as it progresses toward the superior orbital fissure. McKenzie has discussed four theoretical causes for the phenomena in question. It may be due in the first place to hemorrhage in the brain stem; in the second place, from avulsion of the third nerve from the brain stem or pressure of the nerve against the posterior cerebral arteries. He felt that this was the usual explanation for immediate development of the phenomenon. Thirdly, he has explained the disturbance in the majority of cases upon traction of the third nerve around the corner of the clivus by the upper part of the brain stem being pushed to the left, for instance, by a right sided hematoma. Finally, he mentioned hippocampal herniation, but stated that he had not observed it in traumatic cases. Reid and Cone have recently observed such herniation of the hippocampal gyrus in traumatic cases and have confirmed its mechanism by the production of homolateral fixation and dilatation of the pupil by experimental work with monkeys. The autopsy findings in Case 2 amply confirm this report. Bilateral hippocampal herniation has been described by Olsen with attendant pupillary changes in a case of obscure cerebral edema. The conception of central sympathetic stimulation as the causative agent of homolateral dilatation of the pupil in subdural and extradural hemorrhage has been advanced by Schoercher in a recent publication. It may be stated in summary that in an expanding lesion represented by an extradural hemorrhage, transient or permanent dilatation of the ipsilateral pupil is a significant localizing sign, and that the causal mechanism may rest in herniation of the hippocampal gyrus with pressure upon the third nerve.

In the summary of his paper, Jacobson mentioned homolateral paresis as one of seven various manifestations of pyramidal tract defect noted in his cases of extradural hemorrhage, quoting in the body of the paper, Case 52 from F. W. Gross.[1] Among modern studies, the reports of Rand, Vance, and Kennedy and Wortis have mentioned this contradictory neurological finding. McKenzie has stated that homolateral paresis in the presence of an extradural hemorrhage indicates contrecoup contusion of the cerebral cortex. Munro has

[1]Am. J. M. Sc., n. f., vol. 66, p. 45.

stated, "Furthermore, it is not unknown in the later stages of the slowly developing clot, to have a shifting hemiplegia to the ipsilateral side, with a complete reversal of the expected reflex responses." In the mechanically similar condition of acute or chronic subdural hematoma, Holman and Scott, Fleming and Jones, Frazier, Kunkel and Dandy, and Rand have emphasized this peculiar manifestation of the lesion. Its presence has been attributed variously to pressure upon the crus cerebri, a dilated contralateral ventricle, pressure of the contralateral hemisphere upon the cerebral vault and to contrecoup contusion of the cerebral cortex. In 34 cases of brain tumor with false localizing signs of homolateral paresis or pyramidal irritation, Kernohan and Waltman demonstrated notching of the crus cerebri by the free margin of the tentorium. In the case presented, no satisfactory cause for the homolateral paresis could be demonstrated at autopsy.

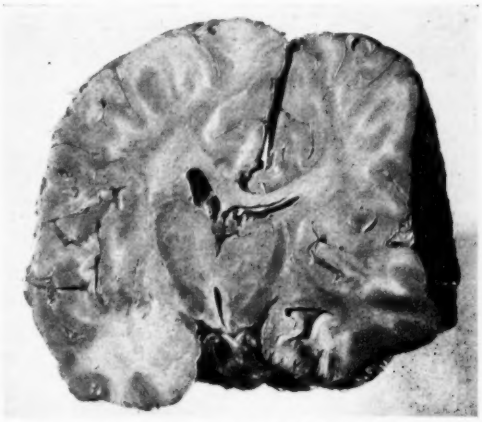

Fig. 3. Extradural hematoma, left. Herniation of hippocampal gyrus. Case 3.

CASE 3. M. C., aged 40 years, history no. 32842. Aberrant form of extradural hemorrhage. History of immediate loss of consciousness in automobile accident 30 minutes prior to admission in the course of a prolonged alcoholic debauch. Laceration and contusion of midfrontal region of scalp. Edema of peri-orbital tissues, left. Persistent loss of consciousness with questionable spasticity and weakness of right sided extremities. Dilatation of left pupil 5 hours after admission. Bilateral spasticity of upper and lower extremities associated with twitching movements. Rapid rise in temperature and pulse with exitus 18 hours after admission. Autopsy: extradural hemorrhage, left. Herniation of left hippocampal gyrus.

A 40 year old colored man was admitted 30 minutes following an automobile accident, totally unconscious. A history of "heavy drinking" was obtained, and a strong alcoholic odor was noticed upon examination. A laceration of the left ear, a laceration of the scalp in the midfrontal region and an edematous discolored left eye were described in the admission summary. There was no clinical evidence of a depressed fracture of the skull. Neurological examination was negative. The patient would occasionally mumble and would move all extremities upon painful stimulation. Five hours after admission, stimulation elicited movement of the left-sided extremities, but on the right, an early paresis seemed manifest. At this time, the left pupil became dilated and fixed and remained so during the course of his admission. Three hours later, there was marked spasticity in both upper extremities with an unsustained ankle clonus on the right. Active dehydration measures were carried out without relief. There was a rapid rise in temperature and pulse rate and the respiratory rhythm became Cheyne-Stokes in character. Fifteen hours following admission, all four extremities were rigid and in extension, although no detailed description of this rigidity is available in the history. Twitching movements of all four extremities are described. Exitus occurred 18 hours following admission.

Autopsy disclosed an extradural hemorrhage, 10 centimeters in diameter and 4 centimeters in width and approximately 3 centimeters in depth in the left temporal fossa with compression of the left hemisphere. There was a linear fracture line in the middle fossa, crossing the vascular channel of the middle meningeal artery 1 centimeter from the foramen spinosum, and passing anteriorly across the wing of the sphenoid bone into the supra-orbital plate. Herniation of the left hippocampal gyrus was present with attendant pressure upon the third nerve (Fig. 3).

The clinical course of this relatively uncomplicated case of extradural hemorrhage illustrates again several points that have been previously discussed. The lucid interval, which has been unduly emphasized in the classical picture of extradural hemorrhage, may be absent because of associated injury or, as in this case, because of complicating acute alcoholism and the rapid development of the extradural hemorrhage. Homolateral dilatation and fixation of the pupil is represented again as an important localizing sign. Finally, the presence of a relative brachycardia in the second case, and an absolute brachycardia in the first and last cases re-emphasizes the importance (47) of a close observation of pulse, temperature, respiration, and blood pressure reactions as early advised by Jacobson. The classic sequence of events depending upon increasing intracranial pressure as postulated by Kocher and Cushing (6) is well known. The validity of this conception has been challenged recently by Shapiro and Jackson, and by Browder and Meyers, the latter authors stating in their discussion of the classic sequence of events, "In the animal, the physiologic alterations in blood pressure, pulse rate, respiratory rate, and intracranial pressure were produced by pressure applied to the external surface of a brain possessed of an intact vascular tree, whereas in the traumatized human brain the lesion producing the dysfunction is usually intracerebral and is commonly associated with focal or more generalized

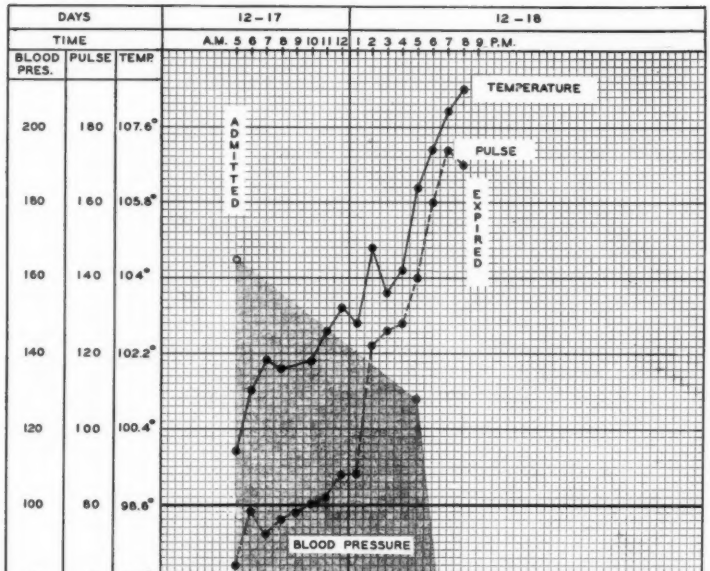

Fig. 4. Extradural hematoma, left. Clinical chart, Case 3.

thromboses of arterioles and venules. Thus it becomes evident that the concept of 'compression' as an explanation of the altered physiologic state of the traumatized patient may be applied in relatively few instances."

The cerebral dysfunction in uncomplicated extradural hemorrhage probably falls into the class of simple compression and proved to be so in the first case recorded as measured by neurological study and lack of postoperative sequelae, and in the third case as measured by histological methods available at the present time for the study of nervous tissue. In all 3 cases reported in this paper the concepts of Kocher and Cushing could be applied with convincing force although it must be acknowledged that repeated mensuration of the spinal fluid pressure was not performed (Fig. 4). It is probable that both increased intracranial pressure, in these cases represented by an expanding extradural hemorrhage, and more subtle pathological intracerebral processes postulated by Browder, may produce the alteration of vital signs detailed by Kocher and Cushing.

The phenomenon of generalized muscular rigidity portrayed in this case has been but infrequently described as a component of the syndrome of extradural hemorrhage, although mentioned by Jacobson in Cases 9 and 59 of his series. It has been observed prior to treatment in one other case of extradural hemorrhage in the Duke Hospital. Jefferson (17) has reported 2 cases in which the usual hemiplegic signs were replaced by a very pronounced degree of generalized muscular rigidity and he refers to the phenomenon as that of decerebrate rigidity citing the paper by Wilson describing the same syndrome appearing in other

circumstances. Inasmuch as the description of the rigidity apparent in Case 3 was not further amplified, Jefferson's description of his second case in his report is worthy of quotation.

"He was then deeply unconscious; the pupils, of medium size, did not react to light. He presented bilateral extensor rigidity of both legs, which were strongly adducted. The feet were in full plantar flexion, inversion, and supination. Every 3 or 4 minutes the tonic contraction of the limb became more pronounced, so that the employment of moderate force was insufficient to separate the thighs. In the intervals between the attacks the limbs were considerably less rigid, so that the legs could be pulled apart and the knees bent, but at no time was there flaccidity, at no time was there an absence of resistance. The left arm during the spasmodic attack was extended stiffly by the side in slight abduction, the wrist was strongly flexed and adducted. The fist was nearly, but not quite, closed and the thumb adducted across the palm within the fingers. The right arm presented a slightly different picture. It was held rigidly bent at the elbow at an angle of 130 degrees, the wrist fully flexed and the hand as on the other side. During the tonic seizures both arms rotated inward into a position of hyperpronation so that the backs of the hands were directed toward the thighs. On the right side this was largely accomplished by an internal rotation at the shoulder joint, the elbow remaining in partial flexion. On the left side, where the whole arm was stiffly held by the side, there was extension and internal rotation of the shoulder aided by pronation in the forearm. An attempt to interfere with the limbs during a tonic attack had little effect, and the muscular contraction was so strong that great force was necessary to restrain the movement or correct the position assumed by its agency. As in the other case, the tonic attacks were closely bound up with a change in the rate and amplitude of respiration. At the height of the attack respiration was rapid, noisy, and deep. As far as one could see, the sequence of events was, first, a change in respiration; next, twitching of the fingers on both sides, rigidity; third, there occurred flexion of the wrist and then inversion of the arms, the legs and trunk at the same time stiffening into extension. During a few of the seizures the patient arched his back in opisthotonos, affecting particularly the lower part of the spine. The head was not seen to retract nor to rotate. There was no incontinence. Ankle clonus was rapid and sustained; plantar stimulation led to a bilateral great toe extension, which was very rapid on the right and slower on the left."

Exploration in this patient was carried out in the right frontal region where a depressed fracture of the skull was elevated; autopsy disclosed an extradural hemorrhage on the left. Jefferson stated that the decerebrate rigidity was due to changes in intracranial circulation produced by the injury. The same conception of generalized muscular rigidity following trauma to the head has been recorded by Babcock, and he has emphasized the serious prognostic import of the findings. Walshe (44) has summarized the characteristics of decerebrate rigidity in man and through such an analysis, has stated that Wilson's cases do not represent true examples of decerebrate rigidity. The same criticism may apply to Jefferson's cases when compared to the classical syndrome as noted in the case reports of Davis and Walshe (45). The latter author (43) considered the phenomenon as a form of generalized chronic muscular spasm due to direct excitation of gray matter in the pons and medulla from oxygen want, stating that "The irritative symptoms which indicate commencing compression of the brain in traumatic intracranial hemorrhage are associated with cyanosis of the brain, that is, deficient oxygenation . . . and "All the evidence indicates that in the primitive character of sensitiveness to oxygen want on the part of the central nervous system, we have a fundamental and potent factor in the production of disordered nervous activity." Whether the phenomenon of generalized muscular rigidity represents decerebrate rigidity or decorticate rigidity or whether it represents simply a premortem rigidity from anoxemia of the medulla, the serious prognostic significance of the finding is clear, and its occurrence in uncomplicated extradural hemorrhage is established.

CONCLUSION

One classical form and 2 aberrant forms of extradural hemorrhage are described and their neurological and pathological manifestations are discussed in this paper. Although Jacobson described aberrant forms of extradural hemorrhage, the modern conception of the clinical syndrome, which had its origin in this paper, is in all probability too rigid. The failure to appreciate the various manifestations of the same intracranial lesion may account for the persistent high mortality and for the large number of cases reaching autopsy without clinical recognition. A dilated, fixed pupil, either of permanent or transient nature, remains the most valuable lateralizing sign, and may, in many instances, be caused by herniation of the corresponding hippocampal gyrus, with pressure on the third nerve. Hemiparesis or other evidence of unilateral pyramidal irritation may be a false localizing sign, caused by pressure of the crus cerebri against the tentorium cerebelli. A careful study of the vital signs may aid in the recognition and further study of simple cerebral compression such as that represented by an extradural hemorrhage. Generalized muscular rigidity, closely approximating decerebrate rigidity, may occur in simple extradural hemorrhage and represents a serious prognostic sign. Its etiology is not established, but may rest upon medullary oxygen want. In view of the demonstrable neurological variability of the clinical picture of extradural hemorrhage, it appears advisable to perform bilateral exploratory trephine in all individuals with acute head injuries when the diagnosis is even suggested.

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UNDERGRADUATE EDUCATION IN FRACTURES AND OTHER TRAUMAS

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FOR a number of years the Committee on Fractures of the American College of Surgeons and now its successor, the Committee on Fractures and Other Traumas, has been attempting to improve the treatment of injury generally throughout this country. As a result of the activities of the numerous regional subcommittees established and kept active in most states of the Union through the untiring and zealous efforts of Dr. Charles L. Scudder, by the publication, revisions, and widespread distribution of the *Manual on the Treatment of Fractures* by the general committee with the co-operation of Dr. Bowman C. Crowell and the College, and through the nation-wide campaign of the Subcommittee on Emergency Treatment and Transportation under the guidance of Dr. Robert H. Kennedy, striking and gratifying improvement in the general handling of the fracture problem has taken place in the last 10 years. There is still much to be done, and the efforts of the general committee and its regional subcommittees will not slacken in the least.

But it has become more and more apparent as the years have passed that a large part of the necessity for the really tremendous effort that this committee has had to put forth lies in the fact that undergraduate instruction in the problems involved in the care of fractures and other traumas has been in general woefully haphazard, unorganized, and frequently distressingly ineffective. Furthermore, instruction in the practical application of the fundamental principles of fracture treatment for internes in our hospitals is frequently lacking or at best on a haphazard basis. More or less voluminous reading and hearsay tested by the "trial and error" method with little or no supervision constitute the fracture education of many of our internes.

Were the treatment of fractures and injury in general a field for the specialist only, the scantiness of instruction for the medical student and the interne would not be of great concern. The perennial discussion as to whether fracture treatment belongs in the field of general surgery or in the realm of orthopedic surgery is futile and purely philosophic. The great run of fractures have always been treated by the general practitioner—the family doctor. They are now so treated, and, unless I am mistaken, they will continue to be so treated. Nor is there any reason why they should not be so treated! The fractures which require the services of a specialist are those presenting problems which cannot be adequately met except by one who has had special training and experience, and who possesses the necessary technical skill, whether he be a so-called general surgeon or orthopedic surgeon. The general practitioner, the general surgeon who sees few fractures, and the orthopedic surgeon who sees but few should all be able to handle adequately the simple case, and to recognize the case which is unusual and which needs special skill and training at the outset—seeing that it gets into proper hands without delay and without a preliminary period of improper or ineffective treatment.

This broad field of the "average" fracture is, for the most part, in the hands of the "general" man throughout this country. Moreover, and particularly with the younger men just out of school and the hospital, the care of these cases constitutes a respectable portion of their annual income. It is no more a specialized field today than is the treatment of pneumonia, heart disease, or gall-bladder colic. The "specialist" is needed in all these cases, and needed badly, when the unusual case provides the need and the "general" man knows what the indications for this need are. We expect him to know this; we teach him to appreciate it as part of his medical school training. But, we also teach him the basic pathology of the disease, its relation to signs and symptoms, course and prognosis, and the principles of treatment involved. We do this by having him see and examine and follow fresh active clinical cases, by demonstrating the pathology in gross fresh or preserved specimens, and by having him see or help in the treatment of the case. We know we cannot hope to do it by a few didactic lectures and the verbal description of an occasional case to an amphitheater full of students.

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Obstetrics is another field in which the specialist is, in general, reserved for the unusual case or for those patients whose resources and location make it possible for them to utilize his services from the beginning. These latter constitute the minority. Again, and rightly so, we train our students by actual contact with patients—active cases—from the beginning. They see, examine, and help in the treatment of actual patients. Were the curriculum in obstetrics to consist of some didactic lectures, with an occasional amphitheater demonstration of a postpartum case and merely a description of what it had looked like before and during delivery, and how delivery had been accomplished, we should rightly feel that medical school instruction in obstetrics was sadly deficient.

The treatment of fractures and other traumas is as much a part of the routine work of the *average general practitioner* as is the treatment of pneumonia and the handling of obstetrical cases.

Injury has its own peculiar pathology of practical importance from the standpoint of diagnosis and treatment indications. The element of time is peculiarly important. The individual make-up of the patient himself holds a place of importance unusual in other conditions. The whole basis of treatment principles is peculiar to the particular pathology of the condition and is based on that pathology and its time schedule.

A survey of the teaching on the diagnosis and treatment of fractures and other injuries in the medical schools of this country reveals that the didactic lecture, the amphitheater demonstration of an all too occasional case—usually after reduction and splinting—with verbal description of what has already been done, and the sometime quizzing on the subject matter of the lectures are the commoner methods of instruction. The number of lectures runs from 3 or 4 to 16 or 17 in different schools; the amphitheater demonstrations from 1 or 2 to half a dozen or more, and the quizzes from none at all to 20 or more. The number of patients seen close at hand before reduction, and the number of reductions and splintings actually so witnessed varies from none in many schools to 20 or more. The opportunity for the student to help in the actual handling of patients varies from zero in some schools to frequent participation in others. In most schools there is no organized course, except a lecture series.

In examining men who come up for appointment as internes or who are taking National Board examinations the lack of knowledge displayed on even the fundamental principles involved in the handling of fractures or other injuries, the vagueness of ideas as to what to do or how or when to do it or why it is done, and the total lack of familiarity with what is going on at the site of injury are distressing and deplorable. Certainly a hospital staff should not have to teach its internes the *fundamentals* of pathology, symptomatology, and the basic principles of treatment.

An aspirant for an interneship who had never examined a chest, or who did not know what a râle sounded like, or who had nothing to go on except an amphitheater lecture demonstration on examination of the abdomen, or who had no knowledge regarding the significance of the pathology involved in varying types of acute appendicitis would stand little chance of winning a place. Yet, when these applicants are asked how many fresh fractures they have seen, how many they have examined, how many they have seen actually treated and followed, the percentage who answer "none" or "one" is astounding.

The subcommittee on medical education is attempting to improve this situation. It is not advisable, or for that matter necessary, at present to ask for more time than is already allowed, at least theoretically, in surgery for the teaching of fractures. What is needed now is definite organization of the time allowed so that each student may receive in the course of his four years at medical school the following instruction: (1) instruction in the correlation between the pathology and repair of fractures and the symptoms and indications for treatment in fractures; (2) instruction in the correlation between the diagnosis and treatment of fractures and gross anatomy; (3) instruction in the basic principles underlying all fracture treatment illustrated by actual patients, as many as possible of whom should be seen by the student while they are receiving their initial treatment; (4) an opportunity to follow some of these patients through the out-patient department long enough to see the results, at least in their early stages; (5) the opportunity, if possible, to see some late results on similar patients; (6) actual instruction and practice in the application of the Keller-Blake and Murray-Jones fixed traction emergency splinting and other forms of emergency splinting; (7) some organized instruction, preferably in the sophomore or junior years, in first aid in general and in the treatment of trauma in general.

It is also felt that the only way this development can be brought about at the present time is through the individual efforts of the men who are doing the actual teaching.

It is the hope of the Committee on Fractures and Other Traumas that in succeeding years,

through the operation of a number of agencies, we may be able to see the above outline of instruction actually carried out with increasingly frequent close contact with the clinical case. If this can be done, a great advance will have been made, the problems of hospital interne instruction will be simplified, and the need for postgraduate instruction greatly lessened. The man who is hurt deserves the same consideration as the man who has pneumonia or as the expectant mother. He cannot get it unless his problem is understood. The basic facts of his problem should be an essential feature of undergraduate and hospital interne education.

RECOGNITION AND EARLY TREATMENT OF INJURIES OF THE GENITO-URINARY SYSTEM

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THE scope of this paper is limited to injuries of the kidney, urinary bladder, and urethra, produced by falls, crushing of the body, and external blows. The deductions and the conclusions were formed from personal experience with 75 cases.

While these injuries comprise but a small percentage of hospital admissions, we are seeing more of them because of the greater number of people carried by motor vehicles and the popularity of vigorous athletics, especially the winter sports.

A serious accident case, especially a patient in shock, presents an immediate diagnostic problem. First, is there a skeletal fracture? A general survey by palpation and roentgenograms should be made; next, a survey of the abdomen is particularly important. Evidences of rigidity, muscle splinting, tumefaction, or localized tenderness give clues to wounded abdominal structure. When hematuria exists the examination should be centered on the kidney, bladder, and urethra.

THE KIDNEY

The structure of the kidney, particularly, lends itself to injury by a compression blow. Its vascularity is rich, its tissue contains little to hold it together, and its capsule is thin and delicate. Suddenly driven against the lower ribs or the stout vertebrae the kidney may tear easily. The terms, contusion, rupture, and pulverizing, describe varying degrees of injury. Sterling and Sands have demonstrated by animal experimentation just how these injuries take place.

There are some factors in this injury which are favorable to healing. One is the ability of bleeding vessels to close themselves by blood clotting. All surgeons are indebted to this phenomenon. Another is the assistance of shock in temporarily lowering the blood pressure and allowing the terminal vessels to collapse.

The symptoms of kidney rupture are severe localized pain, tenderness, muscle rigidity, and a tumor in the flank. Shock is present in 30 per cent.

Hematuria, to some degree, occurs in all cases. Its source is determined by excretion urography, when the patient is not too shocked. An extravasation of the contrast solution or a failure of excretion in one kidney suggests a rupture. Retrograde pyelograms are more specific and better demonstrate small tears. Many patients with renal injuries are able to endure cystoscopy. Whether to operate early or to watch and wait is a question upon which there is a division of opinion.

Eisendrath and Rolnick reported 26 cases of renal ruptures. Three were operated on and 23 treated without surgery, with 1 death. They strongly advocate conservatism rather than early nephrectomy. The author, in a previous study, reviewed 230 cases, found a mortality of 31.9 per cent for those operated on and 3.2 per cent mortality for those treated without exploration. In my own series of 27 cases, 20 recovered without operation. The mortality of the surgical procedures was 27 per cent.

What is expectant treatment? The patient is closely watched for 72 hours. Hourly blood pressure readings are made, an immediate typing classification for blood transfusion and donors available is made and a blood count is done every 2 hours. Transfusions should be given early, as nothing equals them to hasten clotting and over-

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Fig. 1, left. Case 1. B. B., male, aged 20 years. Pyelogram showing rupture of middle calyx, right kidney, mild extravasation of dye, 4 hours after injury.

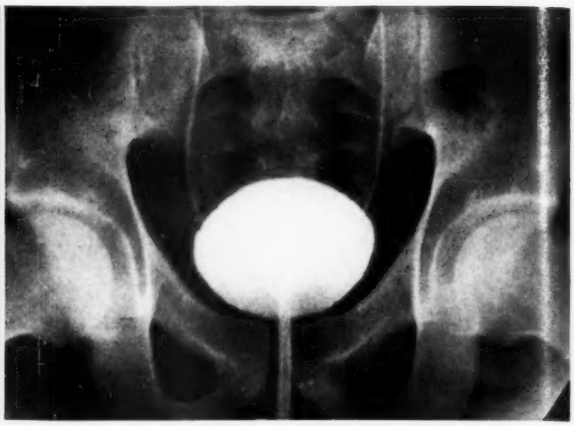

Fig. 2. Same case. Cystogram showing normal bladder contour. No extravasation 4 hours after injury. Recovery 2 weeks.

coming shock. Severe pain is best relieved by heat and morphine. Intravenous urograms or cystoscopy, catheterization of the ureters, and pyelograms should be done as soon as the patient's condition permits.

One contra-indication to immediate surgery is shock. This is often underestimated. I recall the death of an elderly man who suffered a simple fracture of the femur. Autopsy disclosed nothing else. Surgical curiosity must be guarded against. Experience proves that we can well afford to be patient until the shock of the accident has been counteracted. Should tumefaction, extravasation, and infection develop, exploration can then be made. It is amazing to see, at times, a kidney torn in many pieces, yet the hemorrhage stopped by clots.

In cases of vomiting, general abdominal rigidity, and severe pain, exploratory laparotomy is justified and indicated.

Two cases will illustrate the importance of early diagnosis and treatment.

Case 1. B.B., an Oklahoma cowboy, 20 years of age, was brought to King County Hospital on July 21, 1940. At a rodeo meet he fell from and was stepped on by his horse. A hoof fractured the ninth to eleventh ribs, right thorax. He suffered considerable pain. The voided urine was red with blood. His temperature on admission was 98.2 degrees F., pulse 90, and blood pressure, systolic 118, diastolic 70 millimeters. The abdomen was soft, except for muscle spasm of the right costovertebral angle. Cystoscopy showed a normal viscus. The right orifice ejected blood stained urine, the left clear urine. A right pyelogram, using 5 cubic centimeters of contrast solution, showed an extravasation of solution of the middle calyx. A cystogram did not show any leakage from the bladder. We knew definitely the character of the rupture and that conservative nonsurgical treatment was proper. In 3 days hematuria disappeared and on the fourteenth day the patient was discharged. Too early discharge is fraught with danger from delayed hemorrhage.

A case illustrating the more serious type of rupture is the following.

Case 2. A.J.L., a male clerk, 33 years of age, was struck by a streetcar. He was admitted on November 1, 1928, 8 hours after the accident, to Providence Hospital, by Dr. Oscar Proctor. Shock, hematuria, a rigid abdomen, and severe left-sided pain justified an exploration through a left rectus incision. No intra-abdominal lacerations were found. A large, left retroperitoneal hematoma was drained through a secondary loin incision. The kidney was not disturbed. Blood transfusions were administered. The following day the ureters were catheterized. Normal urine flowed from the right one, none from the left. A left pyelogram showed a large area of extravasation. As the patient was gaining ground a waiting policy was followed. Fourteen months later both ureters were catheterized and phenosulphonpthalein intravenous gave 12.5 per cent in 15 minutes from the right kidney, 10 per cent from the left one. One month later the sinus closed. A renal study was made recently. Both kidneys function well, though right ectopia and left traumatic hydronephrosis exist.

The secret of success in this patient was certainty at all times of what was transpiring and knowing that the hemorrhage was controlled. The ability of the kidney to recover from the severest of injuries is remarkable and is probably due to its unrivaled blood supply.

THE URETER

The ureter is seldom injured by blows. It is small in size, elastic, lies in loose connective tissue, and is well protected. It may be torn free

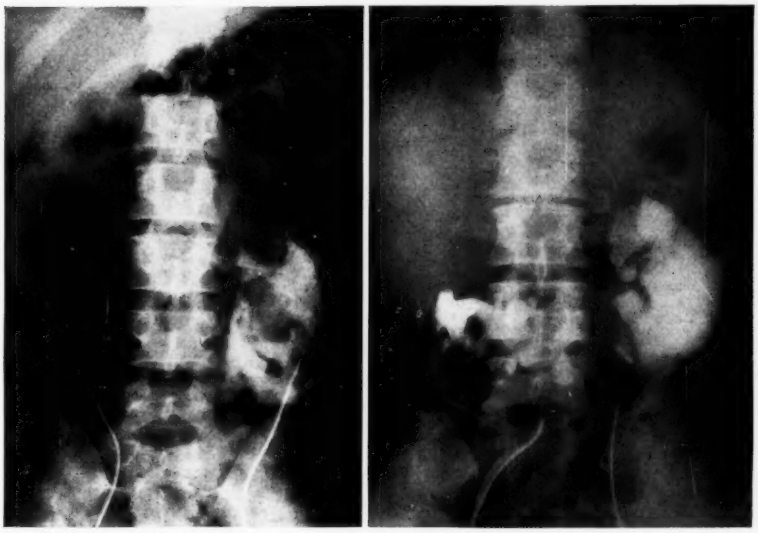

Fig. 3, left. Case 2. A. J. L., male, aged 33 years, clerk. Run down by automobile. Rupture of left kidney with marked extravasation. Twenty-four hours after injury. Recovery 12 months.

Fig. 4. Same case. Rupture of left kidney, 2 years later. Right ectopic kidney and left traumatic hydronephrosis. No symptoms. Recovery 12 months.

at the renal pelvis. It presents few problems in injuries of external origin.

THE URINARY BLADDER

This organ is frequently injured. Two types of injuries are most common. When the bladder is distended, a sudden suprapubic blow, as a kick or falling upon the abdomen, may cause an intraperitoneal or extraperitoneal tear. The other type, is a puncture of the bladder by sharp bone fragments when the pelvis is fractured. These fragments usually cause extravesical extravasation. An empty bladder is rarely injured.

Out of 28 personal cases of ruptured bladder 20 suffered fracture of the pelvis. The cause of accident in this group was 12 due to motor cars, 7 to the logging industry, and 9 to miscellaneous causes.

The symptoms vary somewhat, whether intraperitoneal or extraperitoneal extravasation has occurred.

When shock or alcoholic intoxication exists early recognition is difficult. Suprapubic pain is most significant. Suprapubic dullness, hematuria, and low abdominal rigidity require prompt investigation. A scout roentgenogram of the pelvis to determine fracture, especially of the rami, and a cystogram will make certain the diagnosis. According to Campbell, the mortality of intraperitoneal rupture is high, 73.5 per cent, and that of extraperitoneal, 42.9 per cent, with a corresponding operative mortality. Crane reports a mortality of 40 per cent in 26 cases.

There should be little delay in determining the patency of the bladder. Obtaining clear urine is not conclusive and does not exclude a tear of the bladder wall. Weyrauch and Peterfy report recent animal experiments with cystometrograms. Their results are not convincing as to this method of determining rupture of the bladder. Contrast solution of 5 per cent sodium iodide introduced by a rubber catheter and a cystogram is harmless. Air cystograms are less satisfactory. Intravenous urography again may not show a rupture. If a catheter cannot be introduced an exploratory cystotomy should be made at once. The peritoneum should be opened first, looking for intraperitoneal extravasation. Next, the bladder should be incised and examined. Early cystotomy in all ruptured bladders will cut down the high mortality of this accident. Of 28 personal cases 21 had cystotomies with only 2 deaths, 1 after 8 weeks. Rupture of the kidney can be treated expectantly but rupture of the bladder, never.

Case 3. R.C.T., male, 18 years of age, high school student, was referred by Dr. Park Willis, Jr., Seattle. On

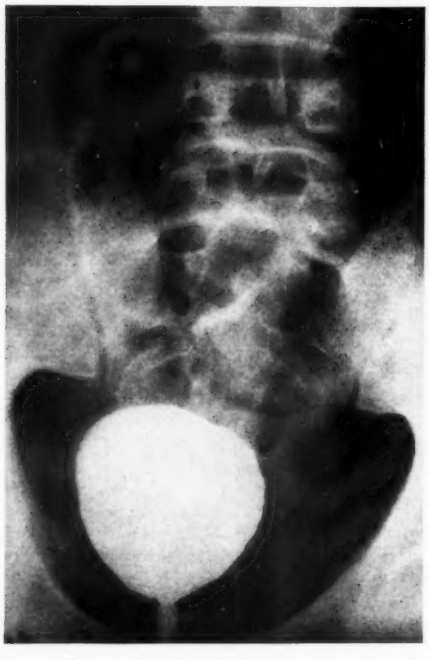

Fig. 5. Case 3. R.C.T., male, age 18 years, student. Automobile accident. Cystogram 12 hours after accident showed small leakage from anterior bladder wall. Cystostomy and recovery in 8 weeks.

December 1, 1939, he was thrown from a coupe in a collision with a second car. He was admitted to King County Hospital at 8:00 p.m. with a blood pressure of 90 systolic and 60 diastolic. Among other symptoms of bodily contusions, he was unable to void. A rubber catheter drew off 2 ounces of bloody urine. He was seen in consultation at 8:15 a.m. the next morning. The blood pressure was systolic 125, diastolic 70, the shock had passed. An interne obtained 250 cubic centimeters of bloody urine by catheter. There was suprapubic soreness and muscle spasm. Roentgenogram showed a separation of pubic bones but no splinters. He was transferred to Seattle General Hospital. At 1:00 p.m. a cystotomy was done, 13 hours after the accident. A tear was found in the anterior wall of the bladder, 2 by 3 centimeters, with extravesical extravasation. Drainage by urethral catheter and a suprapubic button catheter (Pezzer), with gauze drains in the prevesicle space, completed the operation. After a stormy time he was discharged on the forty-second day.

THE URETHRA

Injuries of the urethra result from straddle falls, blows, and kicks to the perineum. Others occur when the urethra is torn by a dislocation of the rami as it passes under the pubic arch. The tube can be sheared off. This disruption may occur at the apex of the prostate. Extravasation

Fig. 6. Case 4. R.W., male, aged 48 years, longshoreman. Crushing of pelvis, bilateral fracture of rami. No cystogram. Rupture of urethra; ischioperineal extravasation. Death on fourteenth day.

takes place as a rule below Colles' fascia, invading the tissue of ischiorectal space, perineum, scrotum, and penis.

These extravasations are particularly vicious and serious infection develops early.

Diagnosis of ruptured urethra rests upon obstruction of the urethra, bleeding from the urinary meatus, inability to micturate, pain in the perineum, marks of trauma, or discoloration and suprapubic dullness and tenderness.

The earlier these cases are seen, the better it is for the patient.

Some injuries of the urethra are mild, with no urethral obstruction except edema and very little bleeding. An indwelling catheter will take care of the traumatism. It should be used for a week or 10 days to counteract the formation of scar tissue.

Rupture of the urethra and extravasation require early drainage of the bladder. Some surgeons prefer the perineal, others the suprapubic incision. Most elect the latter. It keeps the scalpel away from edematous, damaged tissue. By the suprapubic route, a sound may be passed through the urethra and to it can be attached a catheter. This is then drawn out through the urethra and acts as a splint, at the point of rupture.

If bladder drainage is not employed early, serious complications soon arise—hematoma, infection, abscess formation, and spreading of the extravasation through the triangular ligament. Campbell made a study of 135 cases of periurethral infection and noted a mortality of 40 per cent. The longer the extravasation exists, the higher the mortality. Hornaday, Beach, and most urologists strongly stress early surgery.

The following case is the usual picture of delayed interference.

CASE 4. R.W., male, 48 years of age, a longshoreman, was injured by compression of the pelvis. He was caught between two loads of lumber. The injury occurred June 24, 1940. Roentgenograms showed fracture of both rami of the pelvis with displacement. The patient was of large size and the abdomen was distended and tender. A catheter slipped into the urethra and drained clear urine. Later the catheter was withdrawn and he voided. Two weeks after admission, fever, leucocytosis of 23,000 and a swelling of the left inner thigh developed. The following day, July 9, 1940, a perineal incision was made to drain an extravasation. The cavity reached up to the pubic bones, to the site of fracture. The limits of the extravasation were not determined. The patient died the following day and autopsy was not permitted. This patient apparently had a small rupture of the urethra and could have been saved, had an early cystostomy been performed.

It might not be out of place here, to add a word concerning the prevention of these injuries. The motor car has been blamed for many ills yet its use is constantly on the increase. A lesson might be taken from the amusement parks. One of these stunts is a series of small self-propelled cars, guarded by a strong spring-like band, which can bump another car with impunity. The joy rider is further secured by a safety belt. Bumps are the rule but no damage is done. A transportation system, which takes a toll of 40,000 to 50,000 lives a year and injures 200,000, needs some kind of safety study.

SUMMARY

1. Attention to shock is the first step in treatment of genito-urinary injuries.

2. Injuries involving the kidney, bladder, and urethra are relatively rare but serious, and always should be considered in general injuries.

3. Early diagnosis should consist of roentgenograms, urograms, cystograms, and all clinical changes should be carefully recorded.

4. Tears of renal tissue are frequently self-healing and conservatism is better than too early surgery.

5. Tears of the urinary bladder and urethra should have early surgery.

6. Undiagnosed and undetected extravasation of urine results in a high mortality.

7. Motor cars, which are the greatest contributors to serious injuries, need further safeguards, as well as safer drivers.

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FRACTURES DUE TO MUSCULAR VIOLENCE

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IN discussing the subject of fractures recently with some of my colleagues, I found that although they had had a rather large experience with fractures they had not actually seen many instances in which the fracture was produced by true muscular action or violence. A review of a number of recent books and of the literature dealing with the subject revealed that while the opinion exists that various types of fractures may be caused by muscular action or violence, only a very few descriptions or roentgenograms of such fractures appear in these articles or books. With fractures due to muscular violence, I do not include those fairly common, small chip fractures seen at muscular origins or attachments. I refer to the more extensive fractures produced entirely by muscular action in the absence of direct or indirect violence.

I will discuss first 4 cases of fracture of the humerus in the lower third, spiral or comminuted in type, 3 of which were caused by throwing a baseball, 2 by throwing a soft baseball and 1 by throwing a regulation baseball.

In the first case, a man, 31 years of age, while playing in a soft ball game, threw the ball from first base to third base and in doing so fractured the right humerus in the lower third. He heard the bone break and immediately had radial nerve symptoms—numbness and partial paralysis—which later cleared up.

The second case was a fracture of the left humerus in a young woman, who in falling forcibly extended the arm in an effort to catch herself but came in contact with no object.

I consider that in both of these cases the action of the muscles in the shoulder girdle, in combination with those of the upper arm, was the causative factor in producing the injury. The whipping or snapping action of the forearm in the process of throwing while the arm was in abduction, was a factor in producing the fracture. In the woman, to a certain extent, the muscular action may not have been as great as that necessary to throw the ball in the first case, yet the arm was abducted and forcibly extended, so I believe that the forcible extension of the arm was one of the chief factors in producing the fracture.

Presented in the Symposium on Fractures and Other Traumas, before the Clinical Congress of the American College of Surgeons, Chicago, October 21–25, 1940.

These two fractures were of the comminuted type and both had marked radial nerve involvement. In both cases I used the Thomas arm splint, inserted a Kirschner wire through the olecranon under cyclopropane anesthesia, and applied 8 to 10 pounds of traction. The patients were kept in bed. My reason for using this type of treatment was to prevent further radial nerve damage by the continued traction and to prevent if possible the extensive throwing out of callus. After 4 to 5 weeks the arms were put up in plaster-of-Paris casts from shoulder to finger tip, with the elbow at right angles. As union in both of these cases was slightly delayed, the weight of the cast also helped to maintain the position. Both patients obtained good results.

The third patient, another fracture due to throwing a baseball, was treated by Dr. E. S. Allen. While pitching the ball, the patient suffered a spiral fracture of the right humerus, lower third. It was reduced under novocain infiltration anesthesia. There was no comminution but there were radial nerve symptoms. The arm was placed in a Zimmer splint, with the elbow at right angles. The bone united well and there was no permanent nerve involvement. Unfortunately the original x-ray films in this case were destroyed, but we do have a copy of the x-ray report made by Drs. Keith and Keith, which follows:

"Right humerus: Films of the lower half of the right humerus, including the elbow joint, show a spiral oblique fracture 3 inches in length, the center of the fracture being approximately 5 inches above the elbow joint. The distal fragment is rotated and displaced posteriorly approximately 1 centimeter and there is approximately 1 centimeter overlapping.

"Fluoroscopic observation after infiltration novocain anesthesia and several attempts at reduction and several fluoroscopic observations, the arm being fixed in a Zimmer splint, shows good alinement and good approximation of the fragments with no overlapping.

"After permanent dressing had been applied the arm was observed with patient in supine and erect positions, and it appears good reduction has been maintained."

Dr. Charles F. Wood, one of our orthopedic surgeons has permitted me to report, as our fourth case, his personal experience with this type of fracture. While attending medical school, Dr. Wood played soft ball. While pitching one time he felt and heard his right humerus fracture in the lower third. The fracture was spiral in type

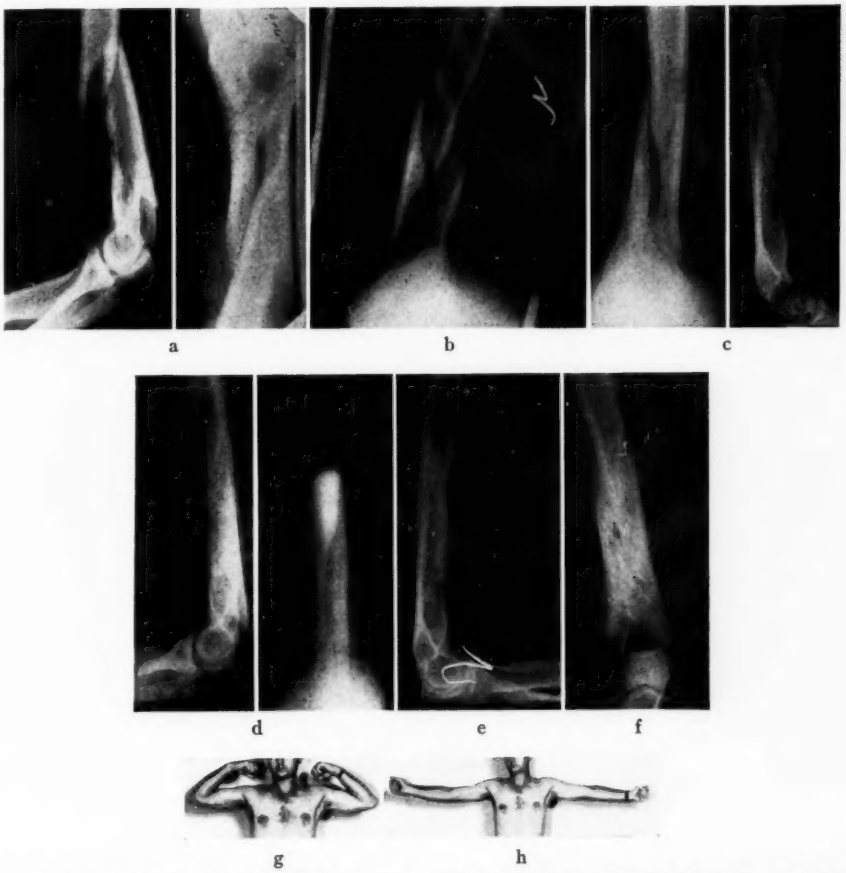


Fig. 1. Case 1. a, Anteroposterior and lateral views at time of injury, fracture at the lower third of the humerus, due to throwing a ball. b, The result of traction after the application of a Kirschner wire through the olecranon. c, Anteroposterior and lateral views taken 4 weeks, and, d, 6 weeks, after application of traction. e and f, anteroposterior and lateral views 1 year after injury; g and h, photographs to show function of the arm and hand 1 year after injury. Radial nerve symptoms which accompanied the fracture later cleared up.

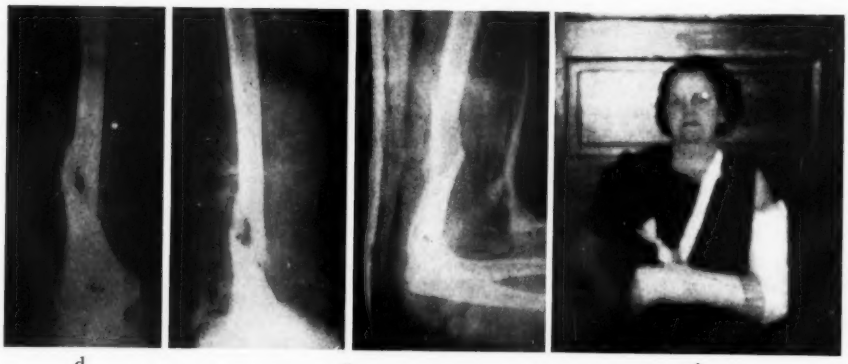
and was associated with a marked and persistent radial nerve involvement, which in the course of time cleared up. Dr. Yandell Roberts had placed the arm at right angles in a plaster-of-Paris dressing, with excellent results. Unfortunately, we can present roentgenograms showing the fracture only as it is at the present time.

The four fractures presented are of a rare type, and I have seen no complete description of them in the literature. While all were complicated by radial nerve involvement, either tingling in the fingers or a partial paralysis, fortunately, the nerve involvement required no surgical intervention and cleared up in all cases.

A fifth case of fracture due to muscular action was seen in a structural steel worker. The man was in a sitting position with his back braced and was helping to push a steel beam into position, with his left leg flexed at the knee; while pushing he felt his patella crack and give way with acute pain in the knee joint. The man had a transverse fracture of the patella, the result of forcible contraction of the quadriceps femoris muscle. It was treated by the usual open surgical operation, and the leg was put up in a plaster-of-Paris cast. He made an uneventful recovery with a good result.

The sixth and last case was that of a young farmer who had a small rural trucking business.

a b c



d e f

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

(*Legends on opposite page.*)

One of his trucks became stuck in a mud hole. While pushing against the truck, he felt something give way in the left lumbar region of his back. This was followed by acute pain. At first, he thought he had lumbago, but eventually a roentgenogram of his spine revealed fractures of the transverse processes on the left side, produced by forcible contraction of the psoas quadratus lumborum and the longissimus dorsi muscles. The patient was treated by rest on a Bradford frame, followed by the application of a back brace. He made an uneventful recovery.

Along with the mechanical treatment, patients are given a high calcium diet, super-D cod liver oil, dicalcium phosphate wafers. Blood calcium estimations, complete blood counts, Wassermann and Kahn tests are made. When it is deemed necessary, basal metabolism readings are also made to determine the dosage of thyroid necessary. We also use all indicated types of physical therapy, massage, diathermy, whirlpool baths, etc.

I have seen no compound fractures due to muscular action. If they were encountered, however, I believe we should treat them as other compound fractures, with gas and tetanus antitoxin, x-ray therapy, sulfanilamide, sulfathiazol, along with properly recognized surgical procedures. I believe that x-ray therapy has a definite place in the treatment of compound fractures whether gas or pyogenic infection is suspected. It apparently does not delay bone union when given in proper dosage. I have had no experience with Dr. Truetas' method of treatment as developed in the late Spanish war.

CONCLUSIONS

Fractures due to muscular violence are not as common as one would suspect. In our series of cases the fractures all occurred in young patients, during the period of life when muscular violence is most common.

Fractures of the humerus which are produced by the throwing of a ball are fairly rare: many surgeons of large experience have never seen a case.

All fractures should be seriously regarded, and, just as in other medical and surgical conditions, all diagnostic methods should be used to determine the extent of the injury and thus to arrive at a decision as to the proper treatment to use in a given case.

I wish to express my thanks to Dr. E. S. Allen and Dr. Charles F. Wood for permitting me to add their cases to this report.

Fig. 2. a, Roentgenogram taken at time of injury, Case 2. b, Roentgenogram taken after traction had been applied by Kirschner wire through olecranon, with arm in Thomas arm splint. c, Patient in bed showing method of traction. d, Fracture coming into position under traction. e, Anteroposterior and lateral views 4 months after injury. Beginning callus formation delayed union. f, Type of plaster dressing worn following the old principle of permitting weight of cast to help maintain position of fracture.

Fig. 3. Case 4. Result (Dr. Wood) at present time. Fracture lower third of humerus due to throwing soft ball.

Fig. 4. Case 5. Transverse fracture of patella in young steel worker due to forcible contraction of the quadriceps femoris muscle.

Fig. 5. Case 6. Fracture of transverse processes due to contraction of psoas, quadratus lumborum, and the longissimus dorsi muscles.

FRACTURES INVOLVING THE ANKLE JOINT

A Classification Based Upon Pathology and Indications for Treatment

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THE subject of ankle fractures, which, for the purpose of this discussion, will include only those injuries of the ankle joint in which the lower end of either the tibia or fibula is fractured with or without displacement of the astragalus, has been well described and is understood by those who have taken any particular interest in the matter.

Ashhurst has classified these fractures into four groups: (1) fractures due to external rotation of the foot; (2) fractures due to abduction of the foot; (3) fractures due to adduction of the foot; (4) compression type of fractures. This is a most excellent classification, and one with which we cannot disagree in any way at all. As a matter of fact, it is such a good classification that it has been copied in most recent textbooks on fractures. However, after ushering a good many groups of internes through their hospital year and discussing the matter with a large number of recent graduates and general practitioners, I believe that the average doctor has a very hazy idea of these injuries. He usually remembers something about a Pott's fracture and is inclined to apply this term and the treatment for the Pott's fracture to practically every injury which occurs within the ankle. This situation, combined with the additional fact that many of these patients are semi-ambulatory from the beginning, and frequently are taken to the office of the nearest doctor rather than to a well equipped hospital, has led to too many disastrous results.

We believe that the reason internes have so much difficulty in remembering the Ashhurst classification is because it is predicated upon the types of force applied to the ankle, rather than upon what has happened to the ankle, and to the additional fact that several types of injury are included in each of Ashhurst's groups. External rotation, we know, may cause a Pott's type of fracture and also may cause a Cotton's type. While the same force may have caused one or the other of two injuries, the type of treatment required is totally different. And, of course, there is also the additional fact that the history is often difficult to get and sometimes not truthful. The result is that the interne, being unable to get a reasonably good story, jumps to the roentgenogram as his only means of diagnosis, forgetting that palpation of the bony landmarks will give almost as much information as any other form of examination. Again, many of these patients are taken to the office of a doctor who has not the benefit of an x-ray machine, and if it appears to be an injury in which the displacement is slight, the condition may be called a sprain of the ankle.

It seems to us, then, that a classification based on the structures injured and the displacement which will or has resulted from the accident is one which would be more easily remembered. If one considers that all fractures of the ankle are produced by forceps so applied that the astragalus is forced or rotated from its normal position with fractures of one or more bony parts of the mortise or rupture of the soft tissues which hold it in position, we can establish at once five types of fractures. They are:

1. Fractures with outward displacement or rotation of the astragalus, or fibular flexion or abduction, whichever term one wishes. This, of course, would include the Dupuytren's and the Pott's, either with fracture of the internal malleolus or rupture of the deltoid ligament.

2. Fractures with inward displacement or rotation of the astragalus, or tibial flexion or adduction fractures. These fractures usually are of the bimalleolar type

3. Fractures with backward displacement of the astragalus, or the Cotton's type of fracture, whether initiated by a straight backward force or rotation, but in which backward displacement of the astragalus is the prime feature.

4. Fractures with forward displacement of the astragalus, a rare type, but one of which we ourselves have four examples.

5. Fractures with upward displacement of the astragalus.

In our experience, all fractures caused by rotation fall into one or the other of these groups. Of course, there are many instances in which the displacement is slight or nil, but it should not be difficult to classify such a case and to select a method of treatment which is suitable. We all

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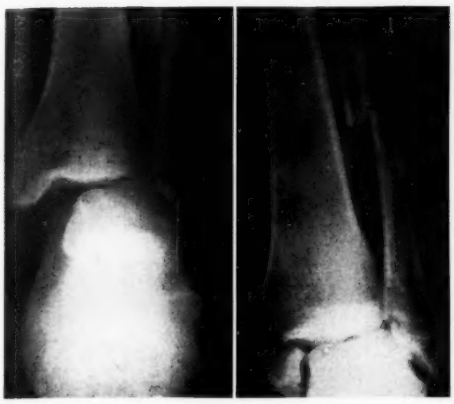

Fig. 1. Two examples of fracture with external displacement of the astragalus. a, left. The internal lateral ligament has been ruptured. b, The internal malleolus has been fractured. Reposition of the astragalus to its normal position is necessary in either case.

know, of course, that in the Pott's fracture the internal lateral ligament may be torn rather than the internal malleolus fractured. And, in case of backward displacement, again the posterior malleolus of the tibia may not be fractured, but, in any case, replacement of the astragalus to its normal position will cause the fragments of bone and soft tissue to fall into place.

Key and Conwell follow this classification in the opening paragraph of their discussion of ankle fractures, but then list the classification of Ashhurst as given above. We have no quarrel with this Ashhurst classification, but, as stated, it seems to us that it is confusing to students and internes.

Diagnosis is accomplished by four methods: (1) observation of the deformity; (2) palpation of the bony landmarks and elicitation of points of tenderness; (3) history, which may be difficult to get truthfully and may come only after leading questions; (4) the roentgenogram, which should never be neglected, but the diagnosis should be made before the plates are viewed.

Treatment

The primary principles of treatment of any of these cases include, first, an accurate reduction, and, second, some means of splinting the ankle and maintaining this reduction until union has occurred. Getting an accurate reduction, of course, means pulling the foot and astragalus back into position in the reverse direction from which it went out of place. That is, in type 1, shoving

Fig. 2. Fracture with internal rotation of the astragalus (bimalleolar fracture with marked supination of the foot).

the foot and astragalus to the inner side; in type 2, shoving it to the outer side; in type 3, bringing it forward; in type 4, backward; and in type 5, downward. If there is any rotation in connection with any one of these deformities, that, then, must be corrected at the same time. Generally speaking, however, all of these patients fall into two groups in regard to treatment.

Types 1, 2 and 4, that is, the types with displacement toward the inner side, displacement toward the outer side, and displacement forward lend themselves very nicely to manipulations under local anesthetic. The patient can be sat up

Fig. 3. Fracture with forward displacement of the astragalus.

a b c

Fig. 4. Fracture with backward displacement of the astragalus (Cotton's fracture). a, The fracture unreduced. b, The fracture only partially reduced. It can be seen that the astragalus will slip off the edge of the tibia with very slight movement. c, The astragalus brought still further forward gives a better reduction.

while this is being carried out, and a skin cast can be applied with the foot in normal relation to the leg and the ankle at 90 degrees. Of course, in compound fractures or in simple fractures in which the skin is in bad condition, skin casts should not be used. If it is necessary to use a padded cast, overcorrection must be carried out. If a skin cast is used successfully, a walking iron can be applied and the patient made ambulatory early, but if a padded cast is necessary, a walking

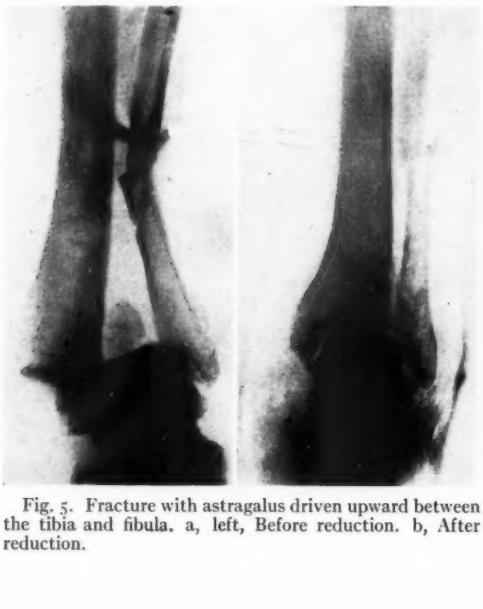

Fig. 5. Fracture with astragalus driven upward between the tibia and fibula. a, left, Before reduction. b, After reduction.

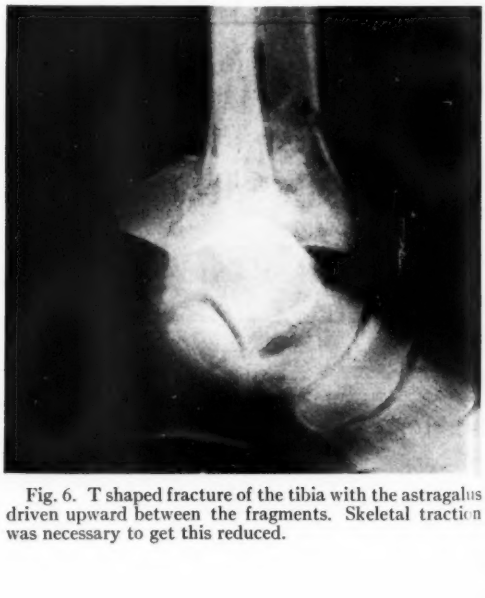

Fig. 6. T shaped fracture of the tibia with the astragalus driven upward between the fragments. Skeletal traction was necessary to get this reduced.

iron is not advisable. X-ray films should be made as soon as the plaster is set, and if the reduction is not satisfactory it should be done over.

In cases of type 3, that is, the backward displacement group or Cotton's fracture, however, it is very difficult to get reduction by manipulation alone, and it is very difficult to maintain the reduction while a cast is being applied. This is particularly true with a local anesthetic, for it must be remembered that if the posterior lip of the tibia is broken off the astragalus slips about upon what is left of the lower end of the tibia very easily. It is very difficult to get a reduction in the first place unless a patient is thoroughly relaxed. We have therefore learned to go immediately to the general anesthetic. The patient can be handled best when he is lying on his face, the knee bent at a right angle, and then with someone holding the leg, the fracture reduced by pulling the foot forward and holding it in that position with the greatest degree of dorsiflexion of the ankle possible, while a plaster cast is being applied. Even with a good anesthetic and a good assistant, it is not always possible to hold the fragments in position long enough to get a cast set. If, after one good honest try, our immediate films show us that we have failed, we think it best immediately to put a pin through the os calcis. Then, with the knee bent at 90 degrees over a frame, to put on strong skeletal traction and at the same time press backward on the leg and forward on the heel, thus get reduction. A cast is applied at once, but the traction is maintained after the patient is returned to bed, the leg having been placed on a bent Thomas or Braun's frame. After about 3 weeks, there is usually enough callus present so that traction can be eliminated and later the pin removed. Even then we do not permit a patient to walk with a walking iron, for we have seen redisplacement of the fragments occur in these cases, even in a well fitting cast. We have heard it said that the only way to get these fractures reduced is to cut the tendo achillis, but with this statement we cannot agree. The tendo achillis was long enough in the first place and will be long enough again. However, one must get a high degree of anesthesia, for if there is spasticity of the gastrocnemius, reduction is impossible. It is further necessary always to put these ankles up with the foot dorsiflexed to the greatest possible degree.

The type 5, or compression type of fractures, are caused by falling from a height, the patient landing on his foot, in which case neither the os calcis nor the astragalus is fractured, but the whole force taken up by the lower end of the tibia. Sometimes the tibia and fibula are separated and the astragalus is driven up between these bones. Sometimes there is a T shaped fracture of the lower end of the tibia with the astragalus driven up between the fragments of the tibia, these fragments lying in front and behind the astragalus; and sometimes only a typical Cotton's fracture is produced. Skeletal traction, as described above, is generally necessary to get reduction in cases of compression fractures. A skin or padded cast is used, depending on the condition of the skin. If a padded cast is necessary, the pin must be left in for a longer time than if a skin cast were used. The walking iron should not be applied until union is fairly firm.

There are cases, of course, which may have been caused by any one of several forces in which there is no displacement. These, if the skin will stand it, are best treated with a plaster cast with the foot in normal position.

CONCLUSIONS

We, therefore, wish to present a classification of these injuries, according to the damage which has occurred, regardless of what force has caused it. We realize it is not as scientific as the Ashhurst classification, but we believe it is one which the average student and interne is more likely to remember. Further than this, the methods of reduction and the indications for treatment are suggested in this classification.

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FRACTURES OF THE TIBIA AND FIBULA TREATED WITH SKELETAL TRACTION AND THE BRAUN-BOEHLER SPLINT

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TYPES of fractures change somewhat with the ages. We no longer see the reverse Colles' fracture so commonly received as a result of backfire of the model T Ford, while cranking the engine. Electric starters for automobiles have eradicated this type of fracture. We seldom now see epiphyseal separation of the femur in childhood, the result of the leg being caught in a revolving wheel of a wagon, carriage, or buggy. The fractures of the horse and buggy days and the model T Fords have gone forever, but in their place have come these fractures due to automobiles, usually of far greater severity than the fractures sustained in the "Gay Nineties."

There is one type of fracture in which the speed of the automobile is not always excessive. This is the so-called "bumper" fracture, the term designated by Cubbins and his associates in 1934, or the "fender" fracture, thus christened by Cotton and Berg.

This type of fracture has received considerable attention during the past few years because of its increasing frequency, and because of the fact that if the deformity is not corrected, it may, as a legacy, leave a deformity which may be embarrassing as well as a handicap—the deformity of genu valgum, "knock-knee," or genu varum "bow legs."

As a result of this type of injury, the patient may sustain a fracture of the external tuberosity of the tibia, if the line of fracture extended into the joint. The French term these fractures as "tibial plateau fractures." There may be an associated fracture of the head of the fibula. The tibial fracture is usually comminuted. There is frequently an associated synovitis or a hemarthrosis of the knee joint, either of which require one or more aspirations to relieve the pain caused by distention of the knee joint. If there is no separation or downward displacement of the fractured external tuberosity of the tibia, the treatment merely involves application of plaster of Paris for immobilization; the unpadded case is extended from the ball of the foot to the thigh with the knee slightly flexed. If, however, there is separation of the fragmented external tuberosity of the tibia or a downward displacement of the fragment, reposition of the separated fragment is essential.

Fracture of the external tibial tuberosity is far more frequent than fracture of the internal tuberosity.

Some surgeons (Eliason, Cotton, et al.) advocate the conservative treatment for this type of fracture and advise against operative intervention. The conservative treatment consists of manual reduction of the displaced fragment and immobilization with unpadded plaster of Paris. Occasionally, if manual manipulation does not suffice, the redresser of Forrester, or the nutcracker of Caldwell, may be helpful with reduction.

The great danger with the use of a redresser, clamp, or the so-called nutcracker is the exertion of undue pressure over the soft tissue which may cause injury to the common peroneal nerve, and result in foot drop (Dixon).

In a recent manual[1] of the treatment of fractures issued by the fracture committee of the American College of Surgeons, soft tissue or skin traction is advocated for the treatment of "bumper" or "fender" fractures. We cannot agree with this suggestion of soft tissue traction, as in our experience soft tissue traction in the treatment of this type of fracture has been of no avail. In any case of "bumper" fracture in which soft tissue traction could be employed, the fracture may equally as well be treated with plaster of Paris with the knee slightly flexed. Soft tissue traction could never be of any avail in a "plateau" fracture with a depressed external tibial tuberosity.

If conservative treatment does not suffice, the surgeon may then resort to reduction and fixation of the depressed or separated fragmented tibial tubercle (spreading fracture) by means of nail, screw, or bone peg. Dyas has advised elevation of the depressed fracture by means of a wedged bone graft placed beneath the lower end of the fragment to wedge it into place. We have never employed this method of treatment, but in selected cases it would appear to be indicated.

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[1]Treatment of Fractures, Committee on Fractures and Other Traumas, 1940, page 44.

Boehler advocates elevation of the fragment by use of a strong metal pin.

The three operative procedures which have given excellent results are the operations of Wheeldon, Buckner, and Webb.

Wheeldon's method consists of the introduction of a Kirschner wire through the separated fragment and the head of the tibia. A sleeve sufficiently long to reach the bone and protrude externally to the skin is introduced, a tightener is applied over each sleeve, and set screws on the ends of the tightener are screwed down securely when the fragment has approximated the head of the tibia. The result is checked by the fluoroscope. When the fragment has been replaced, the ends of the Kirschner wire are cut off, sterile dressings are applied, followed by immobilization by means of a plaster-of-Paris cast extending from the ball of the foot to the groin.

This operative procedure is somewhat less complicated than the procedures of Webb or Buckner, but one of these three operative procedures may be useful in those patients who cannot be properly treated by such conservative measures as to insure against subsequent weakness or deformity of the knee joint.

We have satisfactorily treated these "bumper" fractures with the use of the Braun-Boehler splint and skeletal traction, employing a Kirschner wire through the os calcis. This type of treatment, however, will not restore either the inner or outer tuberosity of the head of the tibia if either is displaced downward. Such deformity requires replacement of the fragment by one of the methods previously described.

We classify fractures of the shafts of the tibia and fibula as transverse fractures, oblique fractures, spiral fracture of the tibia associated with fracture of the fibula, and bimalleolar fractures. In a certain number of fractures of the shaft of both bones of the leg no malposition of the fragment is present. These fractures may be treated by immobilization with plaster of Paris. The knee joint should be slightly flexed to relax the flexor muscles of the leg. This uncomplicated type of fracture, with the exception of fracture of the shaft of the tibia and fibula in childhood, is in the minority. The line of fracture in these cases is usually transverse. The force causing the fracture was not of sufficient intensity to displace the fragments.

More frequently the line of fracture is either transverse, oblique, or spiral, often comminuted. The fragments are usually overlapping. There is associated shortening. With these types of fracture, skeletal traction with a Kirschner wire through the os calcis, the leg being placed on a Braun-Boehler splint, has in the majority of cases been the selected method of treatment.

We have employed the Roger Anderson method of treatment of these fractures with the immediate reduction and the use of pin fixation, followed by the application of a plaster-of-Paris case, but this method has not been as satisfactory as the use of skeletal traction with the employment of the Braun-Boehler splint. With us, this latter treatment has also supplanted open reduction and internal fixation. This latter procedure is only employed when skeletal traction on a Braun-Boehler splint has failed.

The treatment of compound fractures is probably as much of a controversial subject as the treatment of the neck of the femur. There are advocates of débridement followed by the use of bipp paste; débridement with copious irrigation, with primary closure, with secondary or delayed closure; of débridement with the installation of Dakin's solution after the Carrel technique, and advocates of the Orr method. If, in a compound fracture, the injury to the soft tissues is not extensive, the wound may be then irrigated freely and the skin primarily closed. If, however, the injury to the soft tissue is extensive, we employ débridement followed by the installation of Dakin's solution after the technique of Carrel, with skeletal traction and the Braun-Boehler splint.

The advantage of this method of treatment is the ease of dressing the wound, the readiness for x-ray study, and the facility of applying additional traction. No Balkan frame is necessary. The adjustment of a Braun-Boehler frame is less complicated than that of a Thomas splint and Balkan frame.

Skeletal traction with a Kirschner wire through the os calcis and the employment of a Braun-Boehler splint allows mobilization of the knee and ankle of the affected leg.

Some of our more radical surgeons advocating immediate open reduction and internal fixation of fractures of the shafts of leg bones—"from the receiving ward to the operating room" policy—state that this procedure permits immediate mobilization of the knee and ankle. In refutation we would say that many surgeons who follow the open reduction and internal fixation method immobilize the limb in plaster of Paris following operation. It is only the minority that have the temerity not to immobilize after open reduction.

The H. Winnett Orr method of the treatment of compound fractures is advocated by many experienced surgeons. We have seldom employed this method. Results recently published by

Trueta, relating his experiences with the Orr method in the treatment of compound fractures at the Base Hospital in Barcelona, have been so astoundingly satisfactory that this technique demands renewed interest and consideration. The Orr method is certainly far more readily carried out than the method requiring skeletal traction with the extremity immobilized on a Braun-Boehler splint. The Orr method requires less subsequent dressings, so that in military practice, especially, it would seem to be more practical.

During the first phase of the present war in 1918, at the U. S. Hospital No. 38 at Nantes, compound fractures were treated by wound débridement and the installation of Dakin's solution after the Carrel technique with the employment of the Hodgson or Thomas splint. We employed soft tissue traction. No skeletal traction was used at that time. It may be readily appreciated that if the devitalized soft tissues of such compound fractures can be débrided and the extremity immediately immobilized with plaster of Paris, the treatment in military surgery would be greatly facilitated.

Trueta's book is certainly a valuable addition to our knowledge of the treatment of fractures. Whereas it does not advocate any new treatment, yet it certainly emphasizes the value of the conservative Orr method.

BI-MALLEOLAR FRACTURES

Other types of fractures of the lower leg which have been satisfactorily treated with the skeletal traction and the employment of the Braun-Boehler splint, are the bimalleolar fractures and the Pott's fractures, especially when complicated with upward displacement of the astragalus. In these types of fracture we again advocate skeletal traction with a Kirschner wire through the os calcis and the employment of a Braun-Boehler splint.

All cases of fracture of both bones of the lower leg are treated during convalescence with the use of a weight-bearing brace. Our time of bony union has been greatly hastened by the employment of the weight-bearing brace. We have had no case of nonunion; that is, in those cases which we treated from the incipiency of the injury. We believe, however, that such a weight-bearing brace should extend to the thigh, not merely to below the knee.

The average length of time from the infliction of the injury to the application of the weight-bearing brace is about 8 or 9 weeks for fractures of the shafts of the tibia and fibula, and 10 to 12 weeks for bi-malleolar fractures. To allow weight-bearing prior to 10 or 12 weeks for bi-malleolar fractures, especially if patient is heavy or obese, increases the danger of a resulting wide, painful, weak ankle.

CONCLUSIONS

Skeletal traction with the employment of a Kirschner wire through the os calcis, the leg being placed in a Braun-Boehler splint, has been satisfactorily employed in fractures of the tibia and fibula; such fractures include "bumper" or "fender" fractures, transverse, oblique, and spiral fractures of the shaft of the tibia associated with fractures of the fibula as well as bi-malleolar fractures and Pott's fractures complicated with upper dislocation of the astragalus. The treatment has been used for both simple and compound fractures. It is not as radical as the open reduction method with internal fixation. The method is not difficult to apply and does not require the experienced technique of open reduction. In compound fractures the method allows easy access for the treatment of the wound.

In all fractures of both bones of the lower leg the use of a weight-bearing brace during convalescence is strongly advocated.

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OPHTHALMOLOGY, OTOLARYNGOLOGY

THE USE OF HISTAMINE IN MÉNIÈRE'S DISEASE

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THE perfect treatment for Ménière's disease has not been announced nor will it be announced immediately. The story which I have to relate regarding its treatment with histamine is a simple one and can best be told as it actually happened. I do not wish to defend this method of treatment. It will survive or fall on its own merits.

ORIGIN AND DEVELOPMENT OF TREATMENT

CASE 1. On August 5, 1939, a woman aged 44 years, was referred to me because of headaches. These headaches were most peculiar. For about 1 year, she had had attacks of left hemicrania in which the pain tended to extend to the occipital region and even down into the neck and shoulder. During an attack, marked tenderness of the temporal vessels and lacrimation of the left eye were noted. The application of an icebag to the head tended to relieve the pain; the application of heat exaggerated the pain. The attacks, although they sometimes occurred daily, had lasted for only a short time, frequently less than an hour. However, occasionally they had lasted for 24 hours or longer. She had noted that the ingestion of alcohol would precipitate an attack. The attacks invariably came on during the day and never at night. A typical attack was reproduced when the patient was given 0.48 milligram of histamine subcutaneously. The pain which was confined to the left side of the head corresponded to that which had been noted previously during spontaneous attacks. A diagnosis of "histaminic cephalgia" (erythromelalgia of the head) was made (5, 7).

"Desensitization" with histamine was started on the following day and within 15 days the patient was entirely free from headaches and stated that she felt fine.

This patient had had Ménière's disease for more than 4 years and she had been observed at the clinic at frequent intervals during this period; the histamine treatment instituted was not for Ménière's disease but only for the headaches. However, the headache, the tinnitus of the left ear, and the mild attacks of vertigo which she had been having from day to day, all, disappeared. She felt that her hearing also improved. Furthermore, she stated that her head felt clear and the left ear was entirely free from the ringing noise for the first time in 4 years. She was much more elated over the fact that she was free from her vertigo and tinnitus than that she had been relieved of her headache. The heavy feeling back of the left ear disappeared and she was able to stoop over to tie her shoes, turn her head quickly from side to side, and to sleep without a pillow. She was unable to do these things prior to this treatment. Incidentally, she had received ammonium chloride 3 to 4 times daily for the previous 4 years but this had not prevented the attacks of vertigo although it had greatly alleviated them. Subcutaneous injections of histamine were given twice daily for 63 days. During the first 15 days she received 2 injections daily; during the additional 48 days she received only 1 injection of 0.1 milligram daily and remained free from all symptoms of Ménière's disease.

Because of the favorable response to this treatment, 3 additional patients who had Ménière's disease were treated in a similar manner with good results. At a meeting of the Central Society for Clinical Research held in Chicago on November 3 and 4, 1939, H. L. Alexander and R. Elliott, of St. Louis, reported their observations on the treatment of chronic urticaria by means of the intravenous administration of histamine. They were of the opinion that this method was better than the subcutaneous administration of the drug. In view of the fact that I had already obtained good results in Ménière's disease with histamine administered subcutaneously, I felt that perhaps more prompt results might be obtained by the intravenous administration of the drug.

On November 6, 1939, C. H. Shelden and I (8) first treated a patient suffering from Ménière's disease by the intravenous administration of 1.9 milligrams of histamine acid phosphate[1] diluted in 250 cubic centimeters of physiological saline solution. The first patient so treated, who had been confined to bed for a period of 3 weeks because of Ménière's disease, was relieved promptly of all symptoms, was able to get up immediately after the injection was completed and walked about in a perfectly normal manner. This patient has apparently remained well. The first patient referred to in this paper who had been relieved of Ménière's disease by the subcutaneous administration of histamine again returned to the

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[1] In the course of this work histamine acid phosphate and histamine diphosphate have both been used; 1.88 mgm. of histamine acid phosphate or so called histamine monophosphate contains 1 mgm. of histamine base; 2.75 mgm. of histamine diphosphate contains 1 mgm. of histamine base.

clinic on February 19, 1940, because of a recurrence of acute Ménière's disease. She had not taken any histamine for 6 weeks preceding her second visit. On admission she had marked vertigo, nausea, vomiting, and tinnitus which had been present for approximately 12 hours. We immediately started the intravenous injection of histamine. Within 30 minutes, she was free from nausea and vomiting and within 50 minutes the vertigo practically disappeared and the tinnitus was reduced to a marked extent. At the completion of the injection, she was able to get up and walk out of the room. The average acute attack of Ménière's disease which she had had in the previous 4 years had lasted approximately 2 weeks. She has remained well to the present (December, 1940).

DIAGNOSTIC FEATURES IN MÉNIÈRE'S DISEASE

In Ménière's syndrome vertigo is the essential feature and most probably represents a local process involving the labyrinth (8). The factor which is most likely responsible for the syndrome is local alteration in the permeability of the capillary wall resulting in local edema. Histamine is an important agent which affects capillary permeability. The resulting edema may well be comparable to the cotton-wool exudate in the retina and edema of the optic nerve head which are observed in malignant hypertension. Furthermore, it is possible that progressive deafness without obvious cause may be the result of primary involvement of the cochlea. It is comparable to the situation which results when a person who has Ménière's syndrome has recurring attacks of severe vertigo, but without tinnitus or loss of hearing. The degree and extent of involvement of the labyrinth will determine the major presenting symptoms which are observed clinically. This hypothesis seems to be in keeping with the observations of Hallpike and his associates (2, 3, 4). The presence of tinnitus and varying degrees of deafness probably indicates that the process also involves the cochlea.

Caloric tests in determining vestibular function in cases of suspected Ménière's disease may be of some value but certainly are not necessary nor particularly significant in establishing a definite diagnosis. The range of functional activity in this group of cases encountered at the Mayo Clinic varied greatly. Slightly hyperactive reactions on one or both sides were observed in some cases and in others there appeared to be absolutely no response to stimulation. The average reaction would probably be considered to be normal or slightly on the hyperactive side. Most of the caloric tests gave results within normal physiological limits.

I do not believe that diminution of hearing or deafness is necessary before a diagnosis of Ménière's disease is justified. A diagnosis of carcinoma of the stomach can be made in the absence of a palpable mass in the epigastrium and a diagnosis of thrombo-angiitis obliterans in the absence of gangrene. By the same process of reasoning, I feel that a diagnosis of Ménière's syndrome can be made even though the patient has no loss or even diminution in hearing. Loss of hearing, like gangrene and a palpable mass, indicates advanced stages of the disease process.

METHOD AND RESULTS OF TREATMENT

Up to July 1, 1940, the intravenous injection of histamine had been used in 49 cases of Ménière's syndrome at the Mayo Clinic. Thirty-three of the patients were men and 16 were women. The ages ranged from 20 to 69 years for the men and from 28 to 59 years for the women. All had vertigo, 33 had tinnitus, and 32 had some diminution of hearing. All of the patients obtained prompt relief from vertigo, nausea, and vomiting. Less than 50 per cent obtained improvement of tinnitus, the most difficult phase of Ménière's disease to treat. A small number reported improvement in hearing. Twenty-five of the 49 patients previously had undergone some type of Furstenberg treatment. Many of these had obtained palliative effect from this treatment, but the fact that they returned to the clinic for additional treatment indicated that they were not satisfied with the improvement. Some had received no benefit.

CASE 2. A man, aged 64 years, presented himself at the clinic for the second time on March 28, 1940, because of chronic progressive type of Ménière's disease. Symptoms had been present since 1926 and had been much more severe since August, 1938. At the time of his first visit in January, 1939, ammonium chloride plus a low salt diet was advised. Later, he also was given large doses of potassium nitrate. Both forms of treatment failed, however. He slowly became worse for the 14 months he received this type of treatment. He was unable to drive his car, could not move or turn his head quickly from side to side, or lean backward in a chair as it would precipitate vertigo. Following two intravenous injections of 1 milligram each of histamine base in 250 cubic centimeters of normal saline solution, he was unable to bring on any of his previous symptoms. He was able to drive a car and resume his work. He remained entirely symptom-free for 1 month. Since that time he has had occasional mild attacks of dizziness but is not in any way incapacitated.

Our method of treatment of Ménière's syndrome with histamine has not changed materially since Shelden and I originally began this work.

The problem resolves itself, first into eradicating the acute symptoms of vertigo, nausea, vomiting and tinnitus, and this can be accomplished by giving 1 milligram of histamine base (2.75 mgm. of histamine diphosphate) in 250 cubic centimeters of physiological saline solution. This solution is given intravenously at the rate of 50 to 60 drops per minute by the gravity method.[1] It usually requires 1½ hours to administer this amount of histamine. These intravenous injections can be repeated on successive days if the acute symptoms do not subside with the one injection. In acute Ménière's disease, it is usually impossible to give any type of medication by mouth because of the associated nausea and vomiting and yet these symptoms can, as a rule, be eradicated promptly by the intravenous administration of histamine. This is the chief advantage which histamine has over other types of therapy. Some patients seem to get along for months without additional treatment.

CASE 3. A young man, aged 20 years, came to the clinic August 3, 1939, because of attacks of vertigo which he had been having for the previous 3 years. Except for these attacks, his health had been excellent. The attacks of vertigo apparently came on at any time regardless of what he happened to be doing. The onset was sudden and objects seemed to whirl counterclockwise. The severe attacks were accompanied by pallor, cold sweats, nausea, and vomiting. The minor attacks lasted only a few seconds and the more severe ones for half an hour or more. He had had deafness in the left ear as far back as he could remember; tinnitus was not present. He had been on a salt-free diet prior to his admission to the clinic but had had no other type of medication.

General and neurological examinations gave essentially negative results except for complete nerve deafness on the left side. All routine laboratory studies, including a serologic test for syphilis and roentgenogram of the head, gave negative results. He was placed on the Furstenberg schedule and permitted to go home. He derived no benefit from this treatment and returned to the clinic on December 15, 1939, requesting surgical treatment for his condition. Instead, on December 16, 18, and 20, he received intravenous injections of histamine acid phosphate; the dose on each day consisted of 1.9 milligrams dissolved in 250 cubic centimeters of physiological saline solution. At the time of his dismissal from the clinic he was entirely free from vertigo. He had 1 recurrence 10½ months later. He was treated in a similar manner and is now well.

The second phase of the problem resolves itself into the prevention of future attacks. This phase of the work is still in progress, but I feel that an adequate maintenance dose of histamine given subcutaneously 2 to 4 times a week is the best procedure to employ. By an adequate maintenance dosage, we usually mean 0.1 to 0.2 milligram of histamine given subcutaneously 2 to 4 times a week.

CASE 4. A woman, aged 27 years, reported to the clinic November 20, 1939, because of attacks of dizziness and sensations of whirling which had occurred for 18 months. Nausea and vomiting invariably occurred with the sensations of whirling. She was often thrown to the ground during these attacks. Occasionally, she had as many as 4 attacks a day and was incapacitated because of these attacks. Some degree of vertigo had been present since the onset of her illness.

On November 25, 27, and 28, 1939, the patient received intravenous injections of 1.9 milligrams of histamine acid phosphate dissolved in 250 cubic centimeters of physiologic saline solution. All of her symptoms disappeared but the symptoms recurred 3½ weeks later. She received 1.9 milligrams of histamine acid phosphate dissolved in 250 cubic centimeters of physiological saline solution intravenously on December 18 and again on December 19. She was entirely free from symptoms until February 2, 1940. Since that time she has received 0.1 milligram of histamine subcutaneously every other day and she has remained free from symptoms up to the present (approximately 8 months).

TINNITUS

For those who feel that surgical treatment is the only one to employ in Ménière's disease, Case 5 should be of unusual interest. A new method of recording tinnitus is described which should aid in lateralizing the disease and prevent the surgeon from cutting the wrong nerve. It represents a slight modification of the method Baldes and I (6) originally described for recording bruits. Tinnitus, as I have seen it clinically, is of two types. First is the high-pitched noise which patients usually describe as a sensation of escaping steam. If such a noise is identified in terms of frequency per second, it invariably proves to be high, usually of 500 or more vibrations per second. This type of tinnitus should be classified as primarily neurogenic in origin. If the vibrations were plotted, they would form a straight line. The second type is primarily vascular in origin and is synchronous with the heart beat. If the vibrations produced by the noise are plotted, they would form a wavy line. The second type of tinnitus is low-pitched and of less than 150 or even 100 vibrations per second.

CASE 5. A man, aged 44 years, came to the clinic April 3, 1940, because of vertigo, nausea, vomiting, tinnitus and loss of hearing in the left ear of 4 years' duration. The tinnitus, which was subjectively confined to the left ear, had been present for 10 years. He had previously come to the clinic in September, 1939, with similar complaints. Just prior to his second admission, he visited two eminent neurosurgeons, both of whom advised surgical section of the left eighth nerve.

General and neurological examinations at the clinic gave negative results except for marked diminution in hearing of the left ear. The patient stated that he had two kinds of tinnitus in the left ear, one a constant, hissing sound

[1]Ampuls in two sizes are now on the market, one of which contains 2.75 miligrams of histamine diphospate per cubic centimeter (1 mgm. histamine base) and the other 0.275 mgm. of histamine diphosphate per cubic centimeter (0.1 mgm. histamine base).

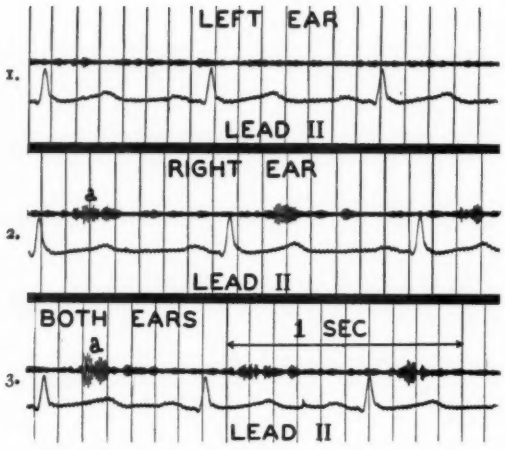

Fig. 1. Recording from left ear, and simultaneous electrocardiogram illustrating lead II. No bruit is present.

Fig. 2. Recording from right ear illustrating a systolic bruit which occurs at *a* simultaneously with the T wave in the accompanying electrocardiogram.

Fig. 3. Recording from both ears illustrating the same phenomena observed in Fig. 2 when the recording was made from the right ear only.

which was high pitched and a coarse rumbling sound which was synchronous with the heart beat. He localized both of these sounds in the left ear. During the time that histamine was being given intravenously, the tinnitus which he heard in the left ear became pronounced. Two stethoscopes were connected so that the ear pieces of one were in the patient's ears and those of the other in the examiner's ears. It was easy to determine the origin of the tinnitus by alternately clamping the tubings from the patient's right and left ears. It was thus easy for the examiner to hear a bruit which originated from the patient's right ear. No bruit was heard from the patient's left ear. This bruit was accentuated with each systolic thrust. By means of a selective sound amplifier, a recording was made first from the left ear (Fig. 1), then from the right ear (Fig. 2), and finally from both ears (Fig. 3). Strange as it may seem, the bruit originated exclusively from the right ear although the patient thought the bruit originated from the left ear. Hearing was reduced in the left ear and normal in the right ear.

This patient had 5 intravenous injections of histamine base of 1 milligram each and then desensitizing injections of histamine were given. He was still having transient attacks of vertigo at the time of his dismissal which was on April 11, 1940. He continued to take 0.1 milligram of histamine base subcutaneously twice a week and on June 12, 1940, he reported that he was evidently well. I saw this patient November 27, 1940, at which time he stated that he was perfectly well.

OBSERVATIONS

At the time this paper was written, 15 of the 49 patients treated with histamine were known to be well. The others have had one or more recurrences of symptoms, possibly because they were not taking a maintenance dose of histamine. In a preliminary report of this type it is impossible to express results accurately in mathematical terms, but rather to express tendencies in terms of treatment. This work is still in progress and much remains to be learned concerning the pathological physiology in Ménière's syndrome but it is my impression that the ultimate treatment will prove to be medical, not surgical.

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THE SURGICAL TREATMENT OF MÉNIÈRE'S DISEASE

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MÉNIÈRE'S disease, or perhaps more correctly Ménière's syndrome, also less correctly known as aural vertigo, is characterized by a sharply defined group of signs and symptoms that is almost pathognomonic. It is one of the most common ailments referable to the cranial nerves. The symptomatic part of the syndrome is as follows: sudden and recurring attacks of dizziness in which objects rotate or oscillate, nausea, vomiting, and tinnitus. The objective part of the syndrome is partial deafness; the tinnitus is on the side of the reduced hearing. The two essential features of the syndrome are: (1) dizzy spells, and (2) deafness. However, only rarely are the other symptoms—nausea, vomiting, and tinnitus—absent in at least some of the attacks. Ménière's disease may be unilateral or bilateral, the latter occurring in about 10 per cent of the total number. When bilateral the two sides may begin synchronously or independently.

Ménière's syndrome was established as a clinical entity by Ménière, a Frenchman, in 1861. He, however, knew nothing concerning its underlying cause, and in the search for a cause confused the clinical picture with that of a case of acute vestibulitis upon which a necropsy was performed. He found what is now recognized as a hemorrhagic purulent exudate throughout the semicircular canals. This, of course, was before the work of Pasteur, who established the bacterial origin of infection, and occurred during a period when hemorrhage was looked upon as the cause of sudden seizures, such as epilepsy. It was, therefore, not unnatural that the hemorrhagic content of the exudate should have been regarded as the cause of Ménière's disease—a concept which has thoroughly permeated the literature and is difficult to overcome even at the present time.

Ménière's disease is doubtless almost as old as the human race. Through descriptions of their characteristic seizures many prominent victims are known for several centuries back. It was in one of his numerous attacks that Martin Luther in an episode that has carried down through the centuries, threw the ink-well at the devil who was violently attacking his ear. Since the latter part of the eighteenth century attacks of this character have frequently been referred to as Dean Swift's disease owing to the fact that this great satirist had so carefully described his own attacks. Throughout the latter half of his life the anticipation and realization of his frequently recurring seizures made him almost a recluse. Among medical men the great Hughlings Jackson was a noted victim. He wrote several articles on aural vertigo, his interest being largely stimulated by his own discomfort. Gamelial Bradford, an American man of letters, so well known for his entertaining biographical sketches, was a victim of Ménière's disease in very virulent form. A vivid description of these attacks which he so aptly calls "the swoop of the hawk" was presented in his journal appearing in *Harper's Magazine* a few years ago.

Pseudo-Ménière's disease is Ménière's disease minus the deafness and tinnitus. In other words, there are the same recurring attacks (in which objects jump and rotate), but there is no indication of the side of the lesion. This condition is by no means uncommon. At times the unilateral features of Ménière's disease develop later. The frequent change from the pseudo-Ménière's to Ménière's disease with time means that in these cases the former is but an early stage of the latter. But that this metamorphosis does not always occur makes it necessary to retain pseudo-Ménière's as a distinct clinical entity.

Symptomatology. In some cases all of the cardinal symptoms of Ménière's disease — deafness, tinnitus, and dizziness — may occur almost synchronously. In other cases any one of the three may antedate the other two for weeks, months, or years. I have seen dizzy attacks grafted upon defective hearing or tinnitus of 20 years' standing. And in other instances after dizzy attacks have continued an equally long time, unilateral deafness and tinnitus have appeared. When dizzy attacks precede unilateral deafness or tinnitus, the diagnosis of pseudo-Ménière's disease must be made.

The dizziness of Ménière's disease (and pseudo-Ménière's) is of a very definite character—objects rotate or jump rapidly. Without dizziness of this type one cannot make the diagnosis of Ménière's disease. Patients who complain of general dizziness with a swooning sensation or an uncertain feeling in the head do not have Ménière's disease. The next essential feature of this dizziness is that it comes in recurring attacks. The onset is usually very sudden, at times so sudden and violent that

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the patient is thrown to the floor and bones may be broken. The attacks last from a few seconds to many hours—even days. The patient must lie down at once and close the eyes but even then only a degree of relief is obtained. I have never known of a patient who could give any precipitating cause. In most instances, and in practically all in the beginning, the patient is perfectly well between attacks. In the later course of the disease there may be a more or less constant state of dizziness, always intensified by movements of the head. The direction of movement or rotation of objects during the attacks has not proved to be of any value in localizing the lesion to one or the other side, i.e., the objects may move in the same direction when the right or left nerve is involved.

Tinnitus. This is rarely absent and is, I think, just as definitely a localizing sign as the deafness. It may be intermittent or constant; it may be intensified before, during, or after an attack, but in perhaps the majority of the cases it is unchanged during the dizzy attacks. The tinnitus varies in its character; it may be a ringing, hissing, or explosive noise. The beginning of tinnitus in the opposite ear is strong presumptive evidence that the syndrome is becoming bilateral.

Deafness. This is nearly always subtotal but in most instances—at least in the relatively late stages that we now see—the hearing is of little practical value. The audiometer curves are quite variable but in most instances all tones are more or less evenly affected. The deafness usually develops slowly and insidiously but it may appear fairly abruptly. It is usually progressive up to a certain point after which it is fairly stationary; however, it may steadily diminish until it is abolished. In about 10 per cent of the cases deafness is bilateral in the beginning or subsequently. Only occasionally is there improvement in the hearing once its downward course begins. At times the hearing disappears suddenly and as suddenly returns, but this is unusual.

Nausea and vomiting. In nearly all cases there is vomiting at some time; it may occur in a few attacks only—usually those that are most severe —or it may be a consistent accompaniment. It may be continuous for days and be scarcely less severe than the dizziness. Nausea is much less constant and is usually more pronounced when the vomiting is severe.

Other symptoms and signs. Various other symptoms are not infrequently present. Diplopia is noted during the attacks in about one-fourth of the cases; no objective evidence of extra-ocular palsies can be observed at the time. Quite frequently patients have a sensation of fullness or a tight feeling in or about the affected ear. There may also be a sensation of a dull, heavy, or even sharp pain which may radiate over the side of the head. I have even seen the pain referred down the arm and chest and from such a pain a diagnosis of angina has been made. It is quite possible that these are referred sympathetic pains. A tight feeling over the chest has been noted a few times. Headaches are not uncommon. They vary in location and severity; some are frontal, others temporal, or occipital.

Following attacks patients may stagger. The staggering may or may not be to one side, and if to one side it is just as frequently on the side opposite as on the side of the affected nerve.

Flashes of light, dark spots, rings, and dimness of vision may occur during and after the seizures. Momentary loss of consciousness occurs occasionally. A singular but constantly recurring complaint in one patient was an intense desire to urinate and defecate so that during the attacks the patient was forced to lie on a bedpan.

Lateral nystagmus, positive Romberg, loss of corneal reflex on the corresponding side, a positive Babinski, and ankle clonus have been occasional objective findings; such findings make one suspicious of an underlying tumor.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

If a patient has recurring attacks of dizziness in which objects whirl or move constantly the diagnosis is either Ménière's or pseudo-Ménière's disease, other signs and symptoms notwithstanding. If there is an additional partial deafness in *one* ear (and the deafness is not due to middle ear infection), the diagnosis is Ménière's disease. If in addition to the dizzy attacks there is partial deafness in both ears, the diagnosis is *bilateral* Ménière's disease. The only other lesion to be considered in the differential diagnosis is a tumor in the cerebellopontine angle and along the eighth nerve. From the 401 patients with Ménière's disease that I have operated upon there have been 3 tumors entirely unsuspected and all were very small. Usually patients who have tumors and Ménière's attacks at the same time show other signs that make the diagnosis of a tumor unmistakable. In the early stages of a tumor's growth and before contiguous structures are implicated, the differential diagnosis would be impossible, for both tumors and Ménière's disease give identically the same objective finding, i.e., partial deafness in one ear. In going over the histories of acoustic and other tumors in the cerebellopontine angle, quite a high percentage gives the typical attacks of Ménière's disease. As a matter of fact the dif-

ferential diagnosis is not so important, for both lesions require the same operative exposure.

ETIOLOGY AND PATHOLOGY

So far as I am aware, in only 2 cases of Ménière's disease has a study been made at necropsy. These were by Cairns, of London, who because of certain histological findings concluded that the cause was in the semicircular canals. This deduction is by no means secure and I think is very doubtful. There is a certain amount of pathological material available from the operative exposures, but since there is no gross lesion in two-thirds of the cases, some doubt remains that one interprets correctly the finding in the minority of cases. That there is an organic lesion is, of course, evident at once from the omnipresent deafness. And deafness is referable to the auditory branch of the eighth nerve and is not responsible for the dizziness, which must be referable to the vestibular branch of this nerve or possibly its end organ — the semicircular canals. Since both the vestibular and cochlear divisions of this nerve are involved, it is evident that the lesion is in the nerve itself and not the end organ—a lesion affecting both the cochlear and the semicircular canals, which are quite a distance apart, would be highly unlikely. It is this fact that causes one to doubt Cairns' conclusion that the lesion is in the semicircular canals. Another reason for assuming that the causative lesion must be in the nerve and not in the end organs is that the attacks are paroxysmal. Unquestionably Ménière's disease is similar in this respect to trigeminal neuralgia and epilepsy. There can now, I think, be no doubt that *only* a cerebral lesion can cause epilepsy, and there can scarcely be a doubt that trigeminal neuralgia is due to a lesion in or on the sensory root, i.e., in both instances a higher neurone, and never a peripheral nerve or end organ, is the site of the lesion causing paroxysmal attacks. A peripheral lesion cannot cause recurring paroxysmal attacks. Operations upon the sensory root of the trigeminus through the posterior fossa disclose a gross lesion in the root in a high percentage of cases—75 to 80 per cent. The lesions are of different kinds—tumors, aneurisms, congenital malformations, and arteries compressing the bare nerve. Similar lesions have been found in Ménière's disease, though in a much smaller percentage of cases—about 35 per cent. In the remaining cases there is unquestionably an intrinsic change in the nerve. From several small pieces of nerve removed at operation there appears to be an increased fibrosis, occurring irregularly and doubtless replacing areas of degeneration in the nerve.

On the other hand, infections that attack the middle ear are probably never followed by Ménière's disease. In the occasional cases in which the semicircular canals (vestibulitis) are directly affected during the extension of a mastoid infection, the dizziness is continuous and gradually abates. I have not seen the recurring attacks of Ménière's disease following the recovery of vestibulitis.

From the negative side it is worthy of note that if Ménière's disease were the result of infections of the middle ear and mastoid sinuses, it would be particularly prevalent in childhood when these infections are so common and when Ménière's disease is almost unknown. Nor is there the slightest evidence to support the thought that focal or systemic infections are directly or indirectly responsible for Ménière's disease. I have never seen an instance of Ménière's disease in which syphilis, tuberculosis, or other chronic inflammatory process was found to be responsible for Ménière's disease, and this despite the fact that bilateral deafness is such a well recognized sequel of syphilis.

Ménière's disease is almost exclusively a disease of middle or more advanced age. This favors its production from thickening of the arteries along the nerves.

For reasons unknown the *left* auditory nerve is the site of these Ménière's attacks about twice as frequently as the right. There is little, if any, difference between males and females.

SURGICAL TREATMENT

Ménière's disease can be permanently cured by division of the auditory nerve. This procedure carries almost no risk to life. Up to the present time I have performed 401 operations, with 1 death—the 358th case—due to meningitis.

Total division of the auditory nerve destroys the remaining hearing in that ear, but that is usually of little practical significance. However, at times it may be important to preserve it, especially when the hearing in the opposite ear is also defective or when the patient's position is dependent upon the preservation of some hearing in both ears, as in certain positions on the railroad. In recent years partial division of the eighth nerve has been used when there is reason to save the remaining hearing. The vestibular branch of the nerve can be divided leaving the auditory branch, and consequently the hearing, intact. There is only rarely a line of division between the two branches of this nerve so that a mathematical division of the nerve is necessary. Usually three-fourths of the anterior part of the nerve is sectioned in order to insure total elimination of vestibular fibers. It has been found that division of

even three-fourths of the auditory division of the nerve does not affect hearing (because of redundant fibers carrying similar functions), and this permits a good margin of safety in insuring destruction of all vestibular fibers that may be included with the auditory fibers. Even so, fractional division of the nerve is attended by a fair percentage (10 per cent to date) of recurrence because the vestibular fibers extend even farther than the line of section. If a patient has bilateral Ménière's or pseudo-Ménière's disease, it is necessary that fractional division be performed on both sides in order to preserve the remaining defective hearing in the one condition, or the normal hearing in the other.

THE OPERATION

Section of the auditory nerve can be done almost painlessly under local anesthesia. There is no sensation when the nerve is sectioned. After the scalp has been procainized the only remaining sensitive area is the under surface of the cerebellum, but by gentle traction the pain is very slight. However, avertin anesthesia is so perfect that I use this almost exclusively. A vertical incision is made along the mastoid and at the tip the incision is curved mesially and downward to a point even with the occipital nerve which can usually be spared. Only a small cut is made through the insertion of the trapezius muscle. The flap of muscle and skin is reflected mesially and then a small circular or oval area of bone is removed with the rongeurs. The bony defect, about the size of a 50 cent piece, is carried laterally as far as the mastoid cells but not into them. If, as occasionally happens, one is opened it should be immediately sealed with wax. After the dura has been opened, the cisterna magna is exposed by retracting the cerebellum and its contents evacuated by tearing a small opening in the leptomeningeal wall. This necessary procedure provides ample room and permits easy retraction of the cerebellum without trauma. The cisterna lateralis is then opened and the contained fluid is aspirated through a suction tube. The eighth nerve then stands in full view. A small hook is gently passed around the nerve which is elevated, thus exposing the concealed seventh nerve. The handle of the hook is then touched with the electrocautery and the nerve is instantly severed. If partial section of the nerve is desired the hook passes under the anterior border of the nerve to the desired point of division and the cautery is applied in the same manner. At times vessels—arteries or veins—in the meninges or even directly on the nerve must be coagulated and divided or pushed aside before the nerve can be safely divided. The facial nerve can, but should not, be injured if the auditory nerve is carefully retracted before its division.

In closing, it is important that the dura be carefully sutured, otherwise intracerebellar hemorrhage might occur from the trauma that results from the thrust of the cerebellum against the edges of the bony opening during vomiting or coughing. Then, too, it is safer to exclude any danger of a cerebrospinal fistula. If the dura is defective a pedunculated or a free muscle transplant (from the under surface of the trapezius) is sutured to the dural margin. When carefully and properly done the procedure is almost without risk.

AFTER-EFFECTS OF DIVIDING THE VESTIBULAR NERVE OR NERVES

If one auditory nerve—or only its vestibular division—is divided there is no permanent loss of vestibular function of any kind. Immediately after the operation the patient may or may not have transient, even severe, dizziness, not unlike a Ménière's attack. When this occurs it usually disappears in a few days. However, there may or may not be dizziness on turning the head for a period of days, weeks, or even months. This, too, always gradually lessens and eventually disappears entirely. Only occasionally does this disturbance continue for any length of time.

Tinnitus may or may not disappear after the nerve is sectioned, and if it persists it may or may not be improved. In about 50 per cent of the cases it disappears completely. One can assure patients that they will never have another attack of dizziness after section of the nerve, if the syndrome is unilateral, but no promise can be made concerning the tinnitus, which a sensible person learns to disregard. There is no staggering gait, and a perfectly negative Romberg after section of one nerve.

Division of both vestibular nerves is attended by one rather surprising after-effect, i.e., jumbling of objects (visual) when the patient is in motion; as soon as the patient is at rest the objects are again perfectly clear. The other disturbance is uncertainty when the patient is walking in the dark. Both of these persist, though with gradual lessening in severity. But both are gladly borne for the relief of the dizzy spells which are no longer possible. These two disturbances indicate the very intimate association between the vestibular and the visual apparatus in human beings. In this connection it is interesting to note that not infrequently during Ménière's attacks and after section of one or both eighth nerves, there is transient diplopia.

Perhaps most surprising is the fact that after both vestibular nerves are sectioned, the gait is normal and the Romberg negative. Doubtless in human beings the cerebellum almost entirely controls this function and has less important dependence upon the semicircular canals; this is not true in animals, to whom the semicircular canals are so important that when eliminated it is impossible to stand or navigate. It is also important to note that when both auditory nerves are sectioned in bilateral Ménière's disease the tinnitus may or may not persist, exactly as with the unilateral type.

Concerning the two types of medical treatment that have been introduced in the past few years, I can only say that very few patients whom I have operated upon in recent years have not tried either or both of them without success. The syndrome is one that lends itself quite well for a time to statistical conclusions because of the marked variations in the frequency of attacks. Some patients will go for months or even years between attacks and what is done last gets the credit for the free interval—*post hoc ergo propter hoc.* I must say that there is nothing in either type of medical treatment but I certainly do believe them to be useless; and I do know that operation cures the disease with almost no risk and with no after-effects.

MEDICAL TREATMENT OF MÉNIÈRE'S DISEASE

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SINCE Ménière, in 1861, first described a disease characterized by recurring attacks of vertigo and unilateral deafness associated with a pathological condition of the inner ear, the exact nature of which is presumed to have been hemorrhage, the eponym has remained in the literature as Ménière's disease. His distinctive contribution was the recognition of the fact that vertigo, nausea, vomiting, deafness, pallor, sweating, and occasional loss of consciousness are due to a lesion in the peripheral vestibular organ and not, as was then held, to a cerebral crisis. Fortunately, Ménière was able to demonstrate a lesion in the labyrinth of a young woman who had died on the fifth day after the onset of these symptoms, although death was probably not caused by the lesion. Ménière also called attention to a tendency for these attacks to recur and to be accompanied by unilateral deafness.

Since that time many reports of similar occurrences have appeared in the literature, until it has been recognized that all cases are not cut to the same pattern, the attacks of vertigo varying in degree of severity and in periodicity of recurrence. Nausea, vomiting, and tinnitus are not always present and vary greatly in degree. For this reason there has arisen a tendency to differentiate the milder attacks which occur without all the recognized symptoms from the disease as originally described, under various pseudonyms, such as Ménière's syndrome, Ménière's symptom complex, paroxysmal vertigo, and recurrent vertigo.

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Northington has put forward a number of cogent reasons for omitting the eponym and has classified the varied manifestations under "peripheral vestibular syndromes," Ménière's disease being recognized as "recurrent vestibular symptoms of obscure or unknown origin." He also points out that the eponym presupposes a condition without any proved pathology and therefore discourages any serious search for a possible etiology. It has been emphasized many times, however, that the condition is not a disease entity in itself but rather a combination of symptoms which may occur with several widely separated lesions, such as pressure on or neuritis of the auditory vestibular apparatus, brain tumors, cardiovascular condition, infectious foci, syphilis, allergy, and so forth.

At the present time, then, it would seem that by the doctrine of good use, the term "Ménière's disease" has come to mean a sequence of signs and symptoms referable to the peripheral vestibular apparatus but without any demonstrable pathology of this organ. Crowe considers that the presence of recurring vertigo alone, without deafness or tinnitus, is sufficient evidence upon which to base the diagnosis.

It seems unnecessary to note any particular violence or frequency of the attacks before the diagnosis is made because every patient complaining of recurrent vertigo should be considered a potential victim of the disease. In this way we

may be able to answer Dandy's query as to whether or not it will be possible to diagnose the condition early in its course and thus conserve hearing in those who have not suffered any previous loss.

PATHOLOGY

While the pathology of the disease is unknown, the symptoms resemble so closely those arising from a stimulation of the labyrinth by the usual tests and an irritation or destruction by inflammatory disease, as to suggest that the peripheral end organs rather than the central ones are at fault. Crowe cites the following reasons, among others, for suspecting the peripheral system: the vestibular symptoms differ only in intensity from functional tests; the infrequency of vestibular symptoms arising from intracranial tumors argues against the disease being in the nerve or the central vestibular nuclei; involvement of other cranial nerves is very rare; choked disc is not present; trauma of the vestibular nerve does not cause symptoms; no pathology has been found in nerves sectioned for study; the strongest reasons for suspecting pressure and chemical changes are the frequency and length of the remissions.

Brunner has contributed an interesting study of the present status of Ménière's syndrome. From an analysis of his own cases of Paget's disease as well as the cases of Hallpike and Cairns and others he concludes that the Ménière's attack corresponds to an attack of otitis interna vasomotoria.

SYMPTOMS

Vertigo. The vertigo of Ménière's disease is characterized by the suddenness of its onset at any time of the day or night, and even during sleep. The violence of the attacks may vary from a slight giddiness to an overpowering vertigo, which immediately incapacitates the subject and may be accompanied by nausea, vomiting, pallor, sweating, diarrhea, and collapse, these symptoms continuing for a varying length of time from minutes to days. If the patient is observed during the attack there is invariably seen a horizontal or rotary nystagmus, the quick component of which may be in either direction but is usually to the healthy side. Owing to the irregularity and short duration of many of the attacks, this symptom is rarely observed.

Deafness. A constant impairment of hearing on one side is always present at some stage of the disease. Cases have been reported in which loss of hearing was not demonstrated until a number of attacks had occurred. It is a not infrequent experience to find that a unilateral deafness has been present for years, either unknown to or forgotten by the patient; however, increased deafness is usually evident at the time of the attack.

Tinnitus. This is a variable symptom. It is often prodromal and is usually unilateral; if bilateral it is more pronounced on the side of the greater deafness. Dandy states that in the presence of bilateral deafness an increase of the tinnitus on one side during a seizure is a definite aid in determining on which side the lesion is to be found.

Labyrinthine tests. It is obviously very difficult to obtain adequate results from these tests during a severe attack. Between seizures the caloric reactions may be normal but are usually somewhat diminished and at times markedly decreased. It is important to realize that whatever the grade of the reactions obtained, they must fall into the normal pattern; any perversion of this pattern must be regarded as indicative of a possible intracranial lesion.

The patient's description of the dizziness is often so indefinite that a comparison of the sensations obtained by the caloric test with that from which the patient suffers is frequently of value in establishing the diagnosis.

DIFFERENTIAL DIAGNOSIS

It seems necessary to discuss only one disease in the differential diagnosis on account of the serious nature of the results which ensue when it is not recognized. The symptoms of an acoustic neuroma in the early stages may strongly resemble Ménière's disease, in that the vertigo and dizziness are of the recurrent type and deafness occurs early. The vertigo, however, is rarely so sudden in onset or so severe in degree as is the case in Ménière's disease; the deafness, however, is of the same type in both conditions. The labyrinthine tests are sometimes of use in the differential diagnosis. Marked or complete loss of all reactions to the caloric test on one side, together with a loss of reactions from the vertical canals on the opposite side, while not pathognomonic, strongly suggests the presence of a subtentorial lesion in the region of the cerebellopontine angle. Later the development of signs of intracranial pressure and of involvement of other nerves serves to establish the diagnosis of an intracranial tumor.

MEDICAL TREATMENT

The literature attests the effectiveness of many methods of treatment, which suggests not only

that the pathology is unknown but also that its causes are variable. Attacks may be so infrequent or vary so in intensity that one applies some method of treatment deemed successful, only to have the symptoms recur with increased frequency and violence. In these circumstances it might be well to adopt the rule used in judging cancer cures, "the five year rule."

To facilitate the discussion of treatment, it is advisable to classify the disease according to its etiological factors. These types are as follows: systemic disease; toxic labyrinthitis, a term in common use among otologists; mechanical type; non-inflammatory lesions of the middle ear; apoplectic type, hemorrhagic and traumatic; Ménière's disease of obscure or unknown origin.

Systemic disease. Symptoms of Ménière's disease may occur in conjunction with some systemic disease, the recognition and correction of which will relieve the distressing symptoms. Northington cites a case with diabetes as the exciting cause, in which relief was obtained by diabetic treatment. Changes in the blood supply to either labyrinth, developing either suddenly or slowly, may upset the equilibrium between the two and cause a considerable disturbance. Sudden anemia or hyperemia brought on by vasomotor disturbances are a not infrequent etiological factor.

Endocrine disturbances may at times have some influence. One case emphasizes the importance of the "five year rule." M.D., suffering from a typical Ménière's syndrome, was found to have a low basal metabolism for which thyroid extract was administered with complete relief of the vertigo for 4 years, at the end of which time the symptoms returned with increased severity. A trial of a low salt diet and ingestion of ammonium chloride proving unsuccessful, complete relief was obtained by section of the nerve.

Vitamins. Avitaminosis as an etiological factor in deafness has been the subject of numerous studies and communications during the last decade. It is not surprising, then, to find that avitaminosis has been identified as a cause of Ménière's disease. Morch and Adams have cited several cases of the disease occurring with a very evident lack of vitamins, in particular vitamin C.

A comprehensive review by Dean before the American Otological Society in 1937 leaves no doubt that allergic diseases of the ear may cause a typical Ménière's syndrome, although the hearing, which is diminished at the time, usually returns to normal.

Treatment of psychosis at times plays a part in lessening the frequency of attacks. S. C. H., 70 years old, had suffered from Ménière's disease 10 years previously but had been free of attacks for 7 years. There was a marked residual deafness on the right side. One year previously the symptoms returned with marked loss of hearing on the left side. Some relief was obtained from a salt free diet and ammonium chloride, but the constant presence of a male nurse by allaying the patient's anxiety did more to reduce the number of attacks. Again, during the bank crisis of 1929 and the ensuing depression many patients presented themselves complaining of dizziness and vertigo which, no doubt, were due to nervous fatigue and an anxiety neurosis.

Toxic labyrinthitis. Foci of infection in relation to Ménière's syndrome have been demonstrated frequently, and otologists as a rule classify this type of Ménière's disease as toxic labyrinthitis. Many cases can be cited in which relief from the symptoms has been obtained by the clearing up of some focus, whether in the sinuses, tonsils, teeth, prostate, or gastro-intestinal tract. Here again it must be emphasized that deafness is a variable factor. Loss of hearing, a sense of fullness, and a buzzing sound in the ear is a usual complaint but is not invariably present at the time of the attack and may occur some time after it. Deafness, if present during the attack, tends to return to normal after the cessation of the symptoms.

Wright has eradicated all foci of infections he could reach in 23 patients. The vertigo was cured in all 23 and in 13 hearing returned to normal.

Mechanical type. Local disease in the middle ear has been shown to cause the symptoms of Ménière's disease. Acute and subacute closure of the eustachian tube has at times been identified as an etiological factor, and inflation of the middle ear is considered by Mygind and Dederding to be an essential part of the treatment. Vertigo and deafness may be brought on by a thin, relaxed, and greatly retracted drum membrane, particularly when the area of greatest retraction is about the incudostapedial joint.

A. N. had suffered from deafness and vertigo for several years, and this had persisted in spite of varied treatments. The drum membrane was found to be draped over the incudostapedial joint, and pressure over this area caused immediate vertigo. The application of a paper splint to the area resulted not only in relief from the vertigo but in marked improvement in the hearing.

Apoplectic type. This type of Ménière's disease is characterized by a loss of consciousness during the initial or subsequent attacks. Ménière's first contributions were his efforts to prove the syndrome to be due to some disturbance of the

labyrinth rather than to a "cerebral crisis," as had been held up to that time. Fortunately, he was able to demonstrate a definite lesion in one of his patients at postmortem examination 5 days after the onset of the initial symptoms. Since then very few complete pathological studies of the labyrinth in this disease were made prior to the report of Hallpike and Cairns in 1938. Politzer apparently considered the apoplectic form of the disease to be always due to hemorrhage. He says:

"Ménière's disease presents itself either with symptoms of an apoplectic form of congestion of the brain, or in the form of a true apoplectic attack. It begins with dizziness, tinnitus, nausea or vomiting, staggering gait, and marked deafness, or the individual falls suddenly with loss of consciousness as if struck down. Consciousness usually returns after a short time."

Treatment of this type is of little avail. Rest and sedatives until the acute reaction has subsided are indicated, and as the opposite labyrinth becomes accommodated all sensations of unsteadiness disappear. The resulting deafness is always very marked or complete, and the semicircular canals fail to respond to stimulation.

Ménière's disease of obscure or unknown origin. The more recent studies of Ménière's disease have stressed the importance of water and mineral metabolism, from which has arisen the theory of retention as an etiological factor. Throughout the literature frequent reference is made to the sudden changes in labyrinthine pressure, either hypertension or hypotension leading to a corresponding hyperemia or anemia. Only in this way can the tendency of the attacks to recur be explained.

Renewed interest in the medical treatment of Ménière's disease has been stimulated by the researches of Mygind and Dederding, who believe that the symptoms are due to increased pressure in the semicircular canals and attribute this increase to a faulty water metabolism which allows water to collect within the cells, resulting in subcutaneous infiltrations and overloading of the fluid in the labyrinth. The variability of the symptoms is explained by the varying amount of retention of the fluids in a predisposed labyrinth; in particular these investigators stress the rapid variations in the ability to learn, which is dependent upon the amount of water retention. They believe that this is a vasomotor phenomenon from which arises a vascular and especially a capillary dysfunction. Their patients "suffer from a peripheral disturbance of the circulation as manifested by chilly sensations, cold hands and feet, vasomotor rhinitis, phenomena which come and go in periods exactly corresponding to the aural phenomena, particularly deafness.

"We maintain," they conclude, "that what we here have to deal with in the subcutaneous infiltrates, in the ear of the Ménière patient, and probably in other parts of the organism, is an edema contingent on a defective function of the vessels, in particular a defective function of the capillaries, an edema which, in a number of important points, distinctly differs from nephritis and cardiac intercellular edema. We have believed that in our patients it was an intracellular edema caused by water leaking out through the enlarged stomata of the dilated paretic capillary wall."

Treatment is directed toward a reduction of the edema by diminishing the fluid intake and by a salt free diet, and also by various physiotherapeutic measures.

These principles are in agreement with the earlier writings of Foldes, who in *A New Approach to Dietetic Therapy* attempts to show that disturbances of the water and mineral metabolism are important pathogenetic factors in a number of diseases, including epilepsy, migraine, bronchial asthma, allergic diseases and hypertension; in 1935 Ménière's disease was added to the list. Foldes contends that water and mineral retention may be present without signs of edema, and, moreover, without apparent cause. Two kinds of disturbance of the water and mineral metabolism are particularly met with in these diseases: "general retention of water and minerals, and mobilization and consecutive local accumulation of water and minerals previously retained through the body." Both retention and sudden mobilization and elimination of retained water and minerals give rise to symptoms, and the treatment, being directed against retention, militates against any sudden mobilization.

In his statement of general principles Foldes says:

"All pathological conditions discussed in this book are distinguished by two peculiarities: (1) that although they present themselves as different phenomena, they are manifestations of one occurrence common to all, i.e., the accumulation of water and minerals in one organ or the other in the entire organism; and (2) that, although besides retention various other factors are necessary to the development of the respective disturbance (local disposition, endocrine constellation, etc.), the accumulation of water and (or) minerals is a condition *sine qua non*."

The general principles of treatment are largely dietary. Use is made of the diuretic effect of a high protein, low carbohydrate and low fat diet, since the last two when given in normal or increased quantities are considered to favor retention of water and mineral salts.

Foldes does not consider a restriction of sodium chloride either feasible or necessary. He holds that salt is not retained if the intake of liquids is restricted but has a diuretic action. Therefore, the only limitation in his diet consists of an

avoidance of distinctly salty foods and of an excess of salt with meals. The amount of liquids to be ingested is limited to about 1 liter, including the fluid content of fruits. The caloric value of the diet is necessarily low, owing to the restriction of carbohydrates and fats. The use of diuretic drugs is not feasible; physical exercise and massage are of value.

Furstenberg, Lashmet, and Lathrop have questioned the accuracy with which the water exchange was measured by Dederding and his associates, and in studies of their own have arrived at the conclusion that the attacks of vertigo occur quite independently of whether water is retained or lost by the body. Furthermore, they found that attacks were produced by the administration of sodium, regardless of whether this was attended by hydration or dehydration. The therapeutic indications are, therefore, to permit as small an intake of sodium as is possible by means of a salt free diet, and to prevent the accumulation of sodium in the body by the administration of acid-producing salts such as ammonium chloride. These investigators report the successful treatment of 14 typical cases of Ménière's disease by this method, all the results being identical. In every case an attack could be precipitated by the administration of sodium chloride. In a later personal communication to Crowe (1937), he says that 125 patients had been treated by this method with splendid results. However, he found it necessary to hospitalize them because of the difficulty in controlling the diet, and because patients are prone to take medicines containing sodium. In 1 case he found that the water supply contained 30 grams of sodium per liter.

The successful results reported by Mygind and Dederding and by Furstenberg attest to value of this treatment. Furthermore the differences in the regimens can be regulated easily, since they occur in the more readily adjustable factors, namely the amount of water intake and the medication.

Finally, a much simpler form of treatment, in our experience over the last year, has proved fully as successful as any heretofore undertaken. Talbott and Brown, recognizing that the regimens of Mygind and Dederding and of Furstenberg were therapeutically successful in spite of their divergent views as to the actual mechanism, became interested in the concentration of electrolytes and the degree of hydration of the blood, both before and after treatment, since neither of these factors had been studied. Their second interest in the study of the blood constituents was particularly the level of the serum potassium. They point out that in a disturbance of conduction of nerve impulses, such as in familial periodic paralysis, a change in concentration of serum potassium is observed and assert that the proper treatment is a high potassium intake. Similarly, symptoms of myasthenia gravis are relieved by a high potassium diet.

In a study of 48 patients suffering from Ménière's disease, the constituents of the blood failed to show any consistent changes from the normal. Furthermore, Talbott and Brown were unable to induce acute attacks in 4 patients by the administration of water or sodium salts. They concluded, therefore, that the therapeutic effect was not achieved by alteration of the concentration of sodium and water in the serum. A further study of the low sodium diet suggested a possible alteration in the proportion of sodium to potassium and if a low sodium diet with a normal potassium content was therapeutically effective, it seemed to them reasonable to try a diet proportionately higher in potassium. To achieve this result, from 6 to 10 grams of potassium chloride in an aqueous solution is given daily, and no other dietary modifications are advised.

Talbott and Brown conclude:

> "In a study of 48 patients with Ménière's syndrome, the concentrations of the acid base constituents of the serum were determined one or more times on 28 patients. The constituents included total fixed base, sodium, potassium, calcium, chloride, total carbon dioxide, phosphate, protein, and non-protein nitrogen. Some bloods were drawn during acute symptoms; others were drawn when patients were relatively symptom-free. No constant variation from normal in the concentration of constituents was observed. Four bloods, however, which were taken during an acute attack showed an increased concentration of serum potassium and a decreased concentration of serum sodium.
>
> "An attempt was made in 4 cases to induce an acute attack. Large amounts of sodium salts were given intravenously and orally in order to produce an increase in concentration of serum sodium. This increase was accomplished in each case without any exacerbation of symptoms. It was concluded that neither hydration nor alkalosis nor an elevated serum sodium is a necessary accompaniment of acute symptoms of Ménière's syndrome.
>
> "The therapeutic effect of this régime has been reassuring. It cannot be considered as a cure for all the symptoms, but clinical improvement has been impressive."

The potassium chloride is administered in a 25 per cent watery solution, each dram containing 1 gram of the salt. The salt is usually well borne, but an occasional patient complains of some distress. Potassium gluconate is tolerated well in larger doses than is potassium chloride and is now readily obtainable.

The precise action of potassium chloride on patients suffering from this disease is not known. Probably the diuretic action of the salt is an im-

portant factor in hastening the excretion of water and sodium chloride. Talbott and Brown believe that "there is a gradual accumulation of evidence which supports the suggestion that the conduction of the nerve impulses is probably associated with an optimal concentration of potassium in the surrounding medium. Any alteration of this concentration may upset a delicate mechanism."

It is apparent that studies in water and mineral metabolism have yielded definite results and still offer a fertile field for investigation. Developments in our knowledge of the vitamins also show promise of increasing usefulness in the treatment of Ménière's disease.

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PRIMARY CARE OF INJURIES OF THE FACE AND JAWS

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INJURIES to the face and jaws vary widely in severity. They may be limited to the most superficial cuts, scrapes, or bruises of the soft tissues. Such wounds, although not serious in themselves, may result in conspicuous scars or deformities when improperly treated.

The more serious injuries are those causing deep, penetrating wounds, or involving fractures of the facial bones. They assume added importance for two reasons: (1) serious complications may develop from a fracture in close proximity to the cranium; (2) gross depressions or deformities even more noticeable than superficial scars may result from injury to the framework, the bone or cartilage of the face.

The result of any such injury may be the cause for much mental distress. The victim of an injury to the face may be permanently hampered by a conviction of unsightliness, whether fancied or real. One cannot overemphasize, therefore, the importance of early adequate treatment of these wounds, whether mild or severe, as the greatest safeguard against serious complications and subsequent deformities. This first aid care can best be given in the hospital. Facilities are generally available to transfer injured patients without loss of time to the accident ward, and therefore in this discussion we will place ourselves in the emergency ward when the accident victim is brought in, bleeding from the nose, mouth, or ears and with lacerations of the face. Obviously, after a hasty examination, the first duty of the surgeon is to control bleeding. Although patients may lose a considerable amount of blood on the way, primary hemorrhage from a cut about the face seldom leads to serious complications. Most lacerations stop bleeding spontaneously under continued pressure maintained with a sterile dressing. However, profuse hemorrhage through the nose from either the septal or the nasopalatine arteries, may be more serious. The procedure in this case is to clean out the blood clot from the nasal passages and pack with sterile gauze saturated with a solution of adrenalin chloride 1:1000. If this is not sufficient, postnasal packing should be resorted to.

After the bleeding is controlled, the surgeon has a better opportunity to examine the patient carefully and make plans for further treatment. Of primary importance is an evaluation of the patient's general physical condition. In certain cases it is best to postpone immediate operation. If the patient obviously is in shock or has lost a large amount of blood, operation should be postponed until transfusion or intravenous fluids have decreased the risk from further surgical trauma. In every serious injury, particularly of the upper half of the face, we must keep in mind the possibility of a cranial injury, and if there are any symptoms pointing in that direction, consultation with a neurosurgeon is indicated.

Bleeding from the nose may be due to a fracture involving the cribriform plate; this may eventually cause leakage of cerebrospinal fluid through the nose. When the latter is mixed with blood it may escape detection. Bleeding from the ears may be due to simple laceration of the tissues of the ear canal, which is not serious, or it may be due to a fracture of the parietal or temporal bones. If there is evidence of brain injury, such as a period of unconsciousness, headache, or vomiting, it is best to postpone any immediate operative measures even though the classical symptoms of shock are absent.

Fortunately, the great majority of injuries of the face are not serious from the standpoint of life and death, and are subject to immediate or early surgical treatment. In this respect, our main object is to re-establish the function of the various tissues of the face and jaws and to eliminate or at least to minimize the visible deformity. Here, even at the risk of oversimplification of the problem before us, I shall discuss the methods used: first, injuries of the soft tissues; and, second, injuries of the bony structure of the face.

INJURIES TO THE SOFT TISSUES OF THE FACE

The ideal time for suturing soft tissue injuries of the face, such as are seen following ordinary automobile accidents, is immediately, or at least within 5 or 6 hours after the accident. At this stage in most cases, active infection has not yet set in. The invasion of micro-organisms from the skin surfaces or the introduction of others by foreign bodies is limited to the surface of the wound and is easily controlled by mechanical cleaning and débridement.

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In treating a superficial wound, the principal aim is to make the resulting scar as inconspicuous as possible. Intelligent surgical procedure will be more readily understood if we analyze some of the problems of wound healing.

1. Other factors being equal non-infected wounds will heal in a better scar line than even mildly infected wounds.

2. Crushed and bruised wound edges become easily infected, and therefore have poor healing power.

3. Children and young adults show a greater capacity to resist infection and the tissues heal readily, but clinical observation shows that they are more prone to the formation of larger scars than are older people. Therefore, we must not be disappointed if a carefully sutured wound later develops conspicuous scars.

4. Certain areas produce better scar lines than others. For instance, lacerations over the forehead, temporal region, over the nose, and to a lesser degree over the chin and immediate neighborhood of the lips show less visible scar lines than those on the cheeks and side of the face. Wherever there is a moderately hard base and dense tissues, the scars will be less visible.

5. The direction of the lacerated wound will somewhat influence the scar line. Horizontal scars over the eyelids are almost inconspicuous, yet vertical scars will invariably cause retraction of the eyelid. Similarly, scars extending parallel to the skin lines are usually the least conspicuous.

6. Long, straight scar lines are generally more conspicuous than broken, "zigzag" lines.

7. Finally, we must remember that what makes the healed wound conspicuous is not so much the presence of the scar as the fact that the scar is likely to disturb the normal contour of the region where it is located. A depressed or elevated scar causes shadows which accentuate its presence. Moreover distortion of the normal outline of the orbicularis oris, the eyelids, or the nostrils resulting from indifferent suturing, from infection, or from contracture of the scar line leads to conspicuous deformities.

Therefore, since we know that we cannot prevent the existence of a scar line, as that is nature's method of repair, our primary aim should be to re-form the tissues so that the normal contours of the face will be preserved.

Operative procedure in primary suturing. In all wounds that are deep, or grossly contaminated by dirt from the street, tetanus antitoxin is immediately given.

The anesthetic of choice for use in the immediate suturing of face wounds, is novocain: either locally infiltrated about the surrounding tissue of the wound, or injected directly into the sensory nerve supplying the region. General anesthesia is used for children and adults of nervous temperament. When the region is thoroughly anesthetized the surgeon is better able to examine the extent of the wound. The first important step in first aid operative procedure is a complete mechanical cleansing of the field of operation with soap and water, and then a careful examination of all the pockets of the wounds for foreign bodies. If a thorough cleansing with soap and water has been done, strong antiseptics such as iodine are not only unnecessary but may be injurious to delicate tissues. The next step is the removal of all the blood clots and débridement—which consists of excision of all the loose particles of tissue and bruised surfaces of the wound. This procedure will eliminate most of the infected tissue and leave a clean cut surface for suturing. Adequate hemostasis is the next important step and cannot be over emphasized. Buried sutures may be used to eliminate dead space and to get good contact of the deeper tissues. When a series of buried sutures are applied to the wound, the skin surfaces should be sutured with many fine stitches without tension. Lately, it has been my routine procedure to avoid straight line suturing in wounds over the mobile parts of the face, and in vertical cuts of the eyelids and lips. Instead I have used a broken line with a series of small "zigzag" flaps. The result has been gratifying particularly in vertical scars of the upper and lower eyelids.

Wounds with loss of tissue. Sometimes in a lacerated wound there is a complete loss of tissue, and if the loss is limited to the skin, one is justified in attempting an immediate plastic closure by means of a free or pedicle graft. However, such cases are usually so infected that it is necessary to postpone repair until a later date.

Late primary suturing. Not all face wounds are clean cut wounds ready for suturing. In fact at the time of hospital admittance a good many wounds are already edematous and infected. There is a great temptation to repair the lacerated tissues as soon as possible, yet one must remember that suturing of even mildly infected wounds never gives a good cosmetic result and complications may even be caused from too early closure.

Therefore, it is fortunate in such cases that there is a broad scope for late primary suturing. This consists of: (1) thorough mechanical cleansing of the wound; (2) applications of frequent hot boric acid fomentations; (3) maintenance of free drainage of the wound. Experience has shown that even badly infected and bruised facial wounds

can be made ready for suturing in from 2 to 10 days by this method.

Powder marks and foreign bodies. Small particles of dirt and powder scattered superficially under the skin present a distressing picture. In some cases the skin has been scraped along in the dirt causing loss of the outer layer of skin in a limited area, with very minute particles of dirt producing discoloration of the bruised area. In other cases, particles of powder are peppered over the face leaving scattered discolored dots over the entire area, often seen in emergency wards following fourth of July celebration. These minute foreign bodies, if not removed immediately, become encapsulated, leaving permanent marks. In a day or two after the accident the points of entry are still open; therefore, it is imperative that vigorous treatment be instituted at this time. Treatment should consist of vigorous mechanical cleansing of the entire affected area with soap and water and a stiff brush, and the marks that are deep and not accessible to bristles of the brush should be scooped out with the point of a sharp knife. To do this, it is necessary to subject the patient to a general anesthetic. It may be a time consuming operation, but it is indicated in view of the gross disfigurement resulting from neglect.

Injuries involving the bony structure of the face. In a short symposium of this type it is obviously impossible to make more than superficial reference to these fractures.

Wounds associated with fractures become a more complicated problem to treat. The patient usually feels the effect of the injuries and has more pain and discomfort, if the external wounds are communicating with a bone injury, which may be contaminated by oral and nasal secretions. Infection takes place more rapidly. However, there is no counterindication to primary suturing in the presence of fractures provided that such a procedure will not block free drainage.

Treatment of fractures of the facial bones. Early and adequate immobilization is perhaps the first principle in the treatment of these fractures. Manipulation is most successful when the fractured parts are loose, as the patient is immediately made more comfortable and the spread of infection is limited. The emergency ward may not, however, be equipped with adequate facilities when special appliances sometimes have to be constructed. A delay of a few hours may not be important but a delay of many days may render reduction of fracture more difficult or impossible; the resulting malposition of the fragments may distort the function of the visual or lacrimal apparatus or create malocclusion of the teeth.

Malar fractures. The majority of malar fractures are simple impacted fractures, the bone being pushed down and back with considerable depression over the zygomatic prominence. No functional disability results from such a fracture if it is left untreated unless the zygomatic arch is pushed against the coronoid process of the mandible. However, loss of the normal prominence of the zygoma is quite conspicuous after the swelling and edema of the soft tissues disappear. The most favorable period for the correction of malar fractures is during the first week following the injury. After that period it becomes increasingly difficult to reduce them.

Comminuted fractures of the malar bone are often associated with fractures of the maxilla. At times, in combined fractures of the malar and maxilla it is impossible to correct the displacement of the maxilla until the depressed malar bone is brought to its normal position. The crushing nature of the injury may cause infection of the maxillary sinus, lower the level of the floor of the orbit or cause permanent diplopia. The main problem in such fractures is to take measures against possible infection of the paranasal sinuses by establishing adequate drainage and immobilization of the comminuted parts by the open method. The maxillary sinus must be opened and drained and all loose or disturbed particles of bone removed. The depressed fragments then may be pulled upward and outward by passing a wire through a drill hole in the infra-orbital ridge and connecting it to a firm headgear with elastic bands.

Fractures of the nasal bones. In discussing fractures of the nasal bones one must include the effect of trauma on the vomer and cartilaginous septum, and lacerations of the nasal mucosa. While the average fracture may not cause any impairment of function, not infrequently the distorted septum and the adhesions of the soft tissues within the nares cause obstruction to the nasal passages. Therefore, in treating nasal fractures I would like to make the following suggestions: (1) Any blow to the nose causing epistaxis requires an x-ray examination, as in simple fractures there is often enough soft tissue reaction to conceal the depression of the nasal bone and confuse the diagnosis. (2) The fracture should be reduced as soon as possible after injury, especially in children as their bones heal very readily, and a postponement of a week may be too late. (3) Fractures involving the cartilaginous part of the septum should be corrected within 24 hours. (4) Lacerations of the nasal mucous membrane should be carefully sutured to their original position and supported with frequent loose packings. (5) Frac-

Fig. 1. Case 1. Bullet wound with early infection and considerable first and second degree bruising and burning. At this stage operation is not indicated.

Fig. 2. Photograph of same patient, taken 10 days after operation.

tures involving both nasal bones and also comminuted fractures should be supported by adequate splints following surgical manipulation.

Fractures of the mandible and maxilla. At present the nature of injuries demands both surgical as well as orthodontic knowledge.

The surgical procedure first of all consists of careful suturing of the lacerated tissue of the buccal mucous membrane. In fractures involving the alveolar process no attempt is made to save broken chips of bone, but these are carefully resected out from the alveolar ridge. The broken down teeth and the teeth involved in the fractured area are also removed. In certain types of fractures of the lower jaw in edentulous patients, direct suturing of the bone fragments is resorted to. However, this procedure is not carried out through an external approach as described in surgical textbooks, but instead, the bone ends are exposed through the oral cavity, which is an easier method and causes less trauma. We are seldom obliged to resort to surgical procedure in fractures of the neck of the condyle when the head of the condyle is driven out of the socket medially. When it is necessary the procedure consists of forcing the condyle back into the socket, but no effort is made to adjust the fractured ends into their normal position.

In general, dental splints for fractures of the maxilla and mandible consist of utilizing the existing teeth as points of retention; if this is not sufficient utilizing the alveolar ridges—the splints resting upon the ridges; external anchorage which is obtained in certain types of maxillary fractures by fitting a headgear over the top of the head; open reduction.

The fundamental aim is to bring the existing teeth into their normal alinement, and this holds true even if there is a definite gap between the two fragments of mandibular bone.

SUMMARY

In conclusion, I wish to emphasize the importance of early and thorough care of injuries to the face. Immediate, gentle cleansing and suturing of clean lacerations will avoid deforming scars. Late primary suturing of edematous infected wounds must always be considered. Early immobilization of fractures will forestall marked irregularities of contour of the face. In all severe injuries the serious consequences of infection penetrating the various sinuses or the cranium must be borne in mind.

CASE REPORTS

Case 1. E. H., female, 15 years of age. This patient was accidentally wounded by a .22 caliber bullet on September 7, 1940. After first aid treatment she was transferred to my care and I saw her about 8 hours after the accident. Examination showed a lacerated wound involving the right and left corners of the mouth and extending through the mucous membrane of the lower lip (Fig. 1). There was considerable bruising and loss of skin at the left corner of the mouth. Most of the upper anterior teeth were destroyed and several of the lower teeth were fractured.

In spite of the fact that effective first aid treatment had been given immediately after the accident, the wound, when seen 8 hours later, was already infected and the tissues about the lips greatly swollen (Fig. 1). Primary suturing, therefore, was contra-indicated. After the wounds were gently cleaned with peroxide and tincture of green soap, warm boric acid fomentations were applied constantly. Antitetanus serum was also administered.

On September 11, 1940, 4 days after the accident, the wounds were sufficiently clean for late primary suturing. Under avertin and ether anesthesia débridement of the granulating tissue of the entire wound was carried out. The bleeding vessels were tied and after considerable approximation and transposition the edges of the wound were carefully sutured.

Fig. 3, left. Case 2. Photographs taken 1 month after primary suturing. Immediate but careful surgery has been carried out, and a good cosmetic result should be obtained.

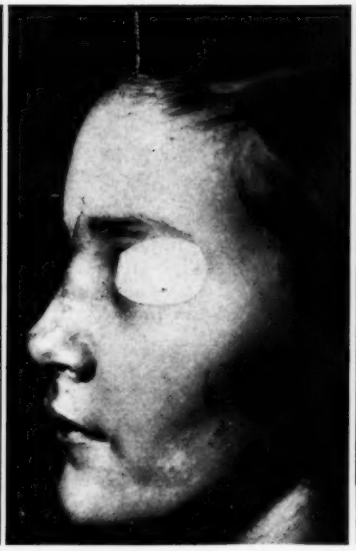

Fig. 4. Photograph of same patient taken 6 years after accident. A secondary lip and nasal plastic operation was performed in addition to primary suturing after injury.

The patient made a good recovery and was discharged from the hospital 9 days after the operation. At this time the scar lines and the moderate distortion of the left corner of the mouth was less than had been expected, and an eventual good cosmetic result could be predicted (Fig. 2).

CASE 2. H. O., female, 16 years of age. This patient was thrown from a horse November 24, 1934, striking her face against a stone wall and sustaining extensive lacerations of the face, in addition to an injury of the spine. She was unconscious for some time. Examination a few hours later showed a deep, lacerated wound extending from the middle of the forehead down over the bridge of the nose and over the upper lip to the vermilion border. Fracture lines which involved the nasal bones and extended down to the maxillary process could be seen quite plainly. The laceration extended into the nasal cavity, separating the mucosa from

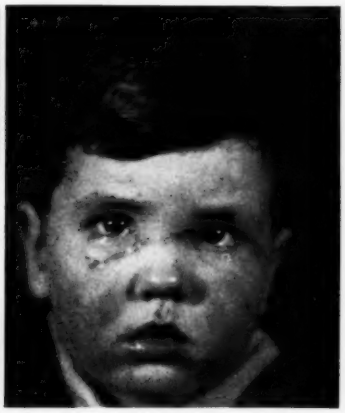

Fig. 5, left. Case 3. Inflamed, lacerated, 48 hour old wound. Operation was delayed another 48 hours. (Delayed primary suturing.)

Fig. 6. Same patient 1 month after operation. There is a good cosmetic result, and still further improvement can be predicted.

the nasal bones. There was a zigzag laceration in the median part of the upper lip penetrating the oral cavity. The septum was fractured and dislocated to the floor of the nose. Several of the upper anterior teeth were loose or fractured.

The patient was operated on the late afternoon of November 24, 1934, under avertin, ether, and novocain anesthesia. The entire face was carefully scrubbed with tincture of green soap and peroxide and the skin painted with merthiolate solution. All the clotted blood and secretions were removed from the nasal cavity with suction tube. The nasal passages were located and packed with gauze saturated with adrenalin. The deep, lacerated wound was then freely exposed and all the clotted blood removed. Three pieces of detached nasal bone were removed and also some small particles of cartilage. The edges of the wound were shaved with a sharp knife and scissors, thus eliminating all the torn and irregular edges. The entire wound including the lip as well as mucous membrane of the nose was then carefully sutured. At first a few deep catgut sutures were applied and the skin was brought together with fine silk. The mucous membrane of the nose as well as the mucous membrane of the mouth was sutured with No. 000 catgut. The left upper lateral tooth which was loose was removed. Rubber dam drainage was applied through the buccal opening of the main wound on the side of the face and sutured to the mucous membrane. The head of the patient was then lowered on the table and the fractured nasal bones and fractured septum were manipulated into position with Asch forceps. The anterior part of the nasal passages was packed on both sides with boric strips to hold the septum in position. External dressing was applied supported by a dental compound mold.

The patient made a good recovery and was discharged from the hospital December 23, 1934 (Fig. 3). She was seen at various intervals, and the scars about the lip and nose gradually became softer. However, there developed some thickness under the upper lip, which gave the appearance of a "double lip" when she smiled. It was decided to operate again to improve the appearance of the lip, and also further to improve the nasal contour.

On June 8, 1935, the patient was operated on under avertin and novocain anesthesia. The "double lip" was corrected by excising a fold of mucous membrane along the inner labial margin; contour of the nose was improved by fracturing both nasal bones and reshaping the bridge.

When this patient was seen in October, 1940, the scar of the face were hardly visible, and the contour of the nose as well as the lip was quite satisfactory (Fig. 4).

The purpose of presenting this case is, first, to emphasize the effectiveness of immediate surgical treatment when the condition of the patient permits such a procedure, and, second, to show that seemingly conspicuous scars following primary suturing will, in the course of time, show considerable improvement.

CASE 3. G. N., male, 3 years of age. This patient was injured in a coasting accident February 24, 1940, when he ran into a strand of wire. This wire cut his nose and face and in addition fractured the nose. The child was unconscious and was treated for shock at a local hospital where hot saline compresses were applied to the wounds of his face. Tetanus antitoxin was also given and the patient was transferred to the Massachusetts Eye and Ear Infirmary 2 days after the accident, February 26, 1940 (Fig. 5).

Examination on that date showed a large gaping wound which extended across the root of the nose toward the center of the right cheek, while on the left side of the face it involved a large area surrounding the inner canthus of the left eye. There was also an extensive laceration over the left temple, close to the outer canthus of the eye, and a comminuted fracture of the nasal bones which were partly exposed. The entire wound was already infected and covered with grayish, granulating tissue; therefore, it was considered inadvisable to perform primary suturing. Constant warm boric acid fomentations were applied, and this procedure helped to clean the wounds.

Two days after admission to the hospital (4 days after the injury) the patient was operated on under general anesthesia. The face was cleansed with soap and peroxide solution. The loose and necrotic tissues were excised by sharp dissection. The skin wound was closed with interrupted kaldermic sutures. A denuded area at the side of the nose leading to the ethmoid cells was left open to granulate in; and the fracture of the nasal bone was reduced in the usual manner. Two small drains were placed deep in the wound for 24 hours. The patient made an uneventful recovery and was discharged from the hospital March 5, 1940, 6 days after the operation (Fig. 6).

THE LATE CARE OF SEVERE INJURIES OF THE FACE AND JAWS

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THE ways in which an injury may be inflicted to the face and jaws are quite diverse, and, therefore, the resultant lesions are of a protean character. Although such injuries in the past were encountered commonly, within recent years they have become more frequent, largely because of automobile accidents. Usually, a woman is the guest passenger when an automobile accident occurs and has not, therefore, the protective support of the steering wheel to prevent a nonsupported forward lurch.

Often, severe injuries of the face and jaws are more tragic than the oftstressed fearfulness of approaching death. Especially, when the victim is a woman, the long years of mental agony that severe facial deformity may cause are deserving of our solicitude; and even in men the psychological handicap imposed by facial disfigurement may blight a promising career.

Whenever the circumstances and condition of the patient permit, most injuries of the face and jaws should be subjected to immediate or early reconstructive procedures. It is, however, common knowledge that often these accidents are complicated by severe injury elsewhere. From necessity, therefore, it may be advisable to delay a reparative operation. The tendency for early swelling to develop and an excessive edema to be manifested after injury is liable to cause the inexperienced surgeon to overlook a depressed fracture of the upper facial region. Careful physical and roentgenological examination, however, should prevent this latter all too common mistake. In the upper jaw region, neglected severe healed injuries are especially difficult to treat. As a rule, however, if the surgeon uses judgment in the selection of the methods at his command, his effort will be well justified.

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The four general procedures which one has at his command in the treatment of these deformities may be expressed briefly as: (1) replacement of displaced soft tissue or bone, (2) substitution of soft tissue or bone, (3) camouflage of the deformity by the addition or the insertion of various substances to build out contour where replacement or substitution is not expedient, and (4) artificial internal or external prosthesis. The general condition of the patient, extent of the lesion after careful physical and, if necessary, roentgenological examination, the availability of the tissue required for reconstruction, age, sex, and status in life are the most prominent factors which will influence the surgeon in the selection of the course which the reconstruction will follow.

Originally, many of the injuries of the face and jaws which present themselves late were of the compound variety. Therefore, in actual practice, the care of the deformity of both the soft and hard tissues must be considered more or less inseparably. But for purposes of discussion, it would seem advisable to speak of injuries of the soft tissues separately from those of the bony structures.

SOFT TISSUE INJURY

After the original lesion has more or less healed, the individuals demanding reconstruction of the soft tissues of the face or mouth are of two types: (1) those in whom there has been little or no actual loss of tissue, and (2) those who have suffered sufficient loss of tissue to require the addition of some substitute material.

In the former group fall those individuals with wide or depressed scars (Fig. 1) and those in whom the soft tissues were not replaced or held in their proper position which may or may not have been properly sutured at the proper time. Following a facial injury, in some instances when the soft tissues of the face are severely lacerated or contused or both, it is advisable either to allow the wound to heal by

Fig. 1. a, left, Result in which the through-and-through incised and also partly lacerated wound of the cheek was rather crudely sutured primarily. Note the stitch scars are at some distance from the incision line and too widely spaced. b, Result 1 year later after careful excision, careful approximation of deeper tissues, and accurate approximation of skin edges plus a mild dose of radium which was given 2 weeks after excision.

secondary intention or to approximate the tissues very loosely. For such lesions, as a rule after careful excision of the scar, mobilization and readjustment of the deeper tissues, followed by proper deep and superficial approximation and resuturing of the wound, satisfactory contour and a hairline scar of the skin may be offered (Fig. 1, a and b).

When suture marks are present following careless primary suture or late withdrawal of the sutures, the surgeon is likely to be more embarrassed because of the suture marks (Fig. 2) which cannot be removed than by the scar of the primary injury which as a rule can largely be obliterated.

Healed "trap-door" flaps, because of the original bevelling of the edges of the flap, present a special problem (Fig. 3, a and b). Due to the underlying scar with its tendency to undergo contraction and the thin edge of the derma which tends to shrink, a humped-up pad of skin and subcutaneous tissue surrounded by an unsightly scar tends to form. Usually, one may repair this deformity by reraising the flap, excising the underlying scar, and removing the circumferential epithelial and dermal edge so that a right angled skin edge is obtained. The outside circumferential epithelial rim also should be cut to a right angle. Two small V-shaped excisions may be made at either end of the horseshoe-shaped external circumference to limit its length. The skin edges of the two horseshoe-shaped incisions should be carefully approximated, and a pressure dressing applied. This should be left *in situ* for 10 days.

Fig. 2. Severe cut across face in which stitch marks are more likely to embarrass the surgeon when he attempts a secondary repair than the scar in the suture line.

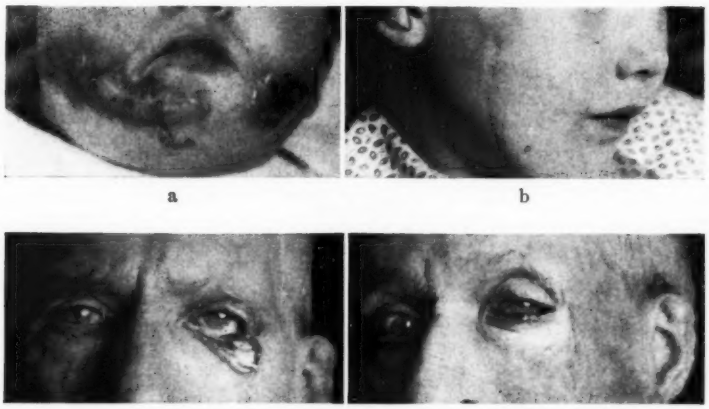
To gain a satisfactory reconstruction in that group of individuals in whom the loss of soft tissue has been considerable, the surgeon must take into consideration the breadth and depth of the loss and whether or not the full thickness of some structure, such as the ala, cheek, or lip, has been destroyed (Fig. 4, a, b, c, d). For the repair of large surface defects, generally a skin graft of a suitable size and thickness for the area and region to be covered is preferable to a skin flap (Fig. 5, a and b). When, however, a swinging advancement skin flap from the immediate neighborhood as advocated by Esser and Imre is utilizable, it will sometimes give the most perfect result obtainable because of the natural texture and color

Fig. 3. a, left, "Trap door" flap of lip and nose. The surgeon was handicapped at the time of the operation by the amount of edema and swelling. b, Result several months after rearrangement of tissue as described in text for "trap-door" flap.

a b c d

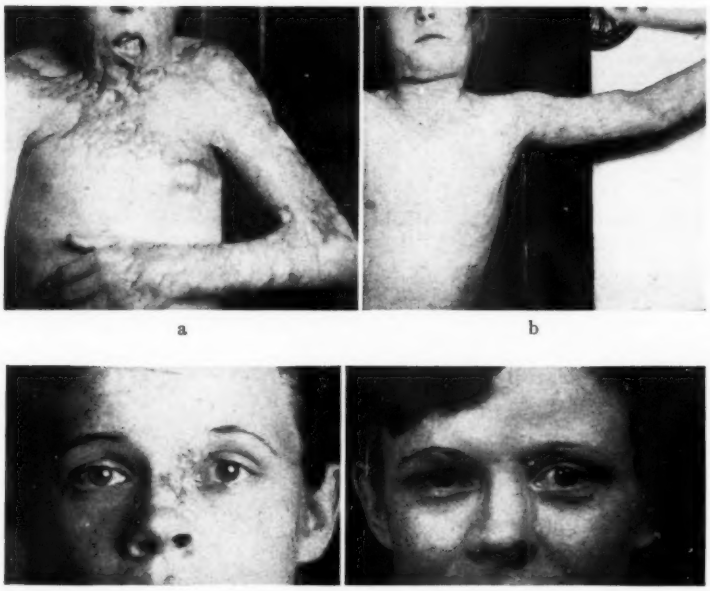
Fig. 4. a, Loss of about two-thirds of lower lip. An artery flap from the left upper lip and cheek consisting of full thickness of lip and cheek was turned into lower lip defect. It is possible this could have been done early. b, Result 3 months after operation. c, Almost one-third of full thickness of nose was removed. Lateral nose rebuilt by means of a skin flap from the forehead. The flap was lined with a thick skin graft. d, Result 6 months after completion of operation.

of the skin of the advanced flap. For the repair of surface defects such as those causing ectropion of the eyelids (Fig. 5, c and d) in which the circular fibers of muscle are near the surface (orbicularis palpebrum and orbicularis oris), a comparatively thin skin graft is preferable. In the past, thin skin grafts have been considered preferable for the correction of ectropion of the lip, but since the development of the calibrated deep intermediate skin



a b c d

Fig. 5. a, Keloidal scar of face. Scar excised and thick skin graft applied. b, Result a few years after operation. c, d, Marked ectropion of lower eyelid and scar of left cheek. Correction made by means of a thin skin graft applied over a stent.



a b c d

Fig. 6. a, b, Photograph of patient with marked cicatricial contracture of the lower mental region, the neck, the upper chest, the right axilla, and the right elbow region. Three operations were necessary to correct this deformity and deep intermediate skin grafts, .018 of an inch in thickness, were used to correct the contractures. At each operation, good "takes" occurred but there was a certain amount of subsequent contracture. The photographs show patient before operative procedures were instituted and 4 months after the last operation. c, Contoural deformity of the nose repaired, and contour re-established by means of a skin flap from the forehead. d, Result several months after completion of operation.

Fig. 7. a, left. This man had lost a good part of the supraorbital ridge and frontal bone. Correction was made by laying back skin flaps over the area and inserting a cartilage transplant of the proper shape to bring out the contour. b, Result 2 weeks later before the eyebrow grew.

Fig. 8. a, left. Lateral deviation of nose due to lateral blow. Result after chiselling the nasal bone from the maxillary processes. Two weeks after operation, a head cast was applied into which a doubled wire was inserted in such a manner as to press on a felt pad over the lateral side of the nose to hold it in position (see Fig. 9). b, Result several months later.

graft cut in the last quarter thickness of the skin, practically all facial surface defects of any size, save those of the eyelids, have been resurfaced with this new graft with results very much superior to those previously obtained (Fig. 6, a and b).

When there is a moderate contoural defect, a skin flap usually will give a result preferable to a skin graft (Fig. 6, c and d.). The contention of Maliniak that if one takes a flap crosswise of the forehead and pulls the neighboring skin together by successive steps without using a skin graft to cover the forehead defect practically no scar is left on the forehead, is a point of value when considering the site from which one is to obtain the skin flap.

For the reconstruction of organs, for building a part requiring two soft, pliable, epithelial

Fig. 9. a, Head cast with doubled wire insert so as to lie alongside the nose. A felt pad is inserted beneath the wire—an efficient and economical appliance which may be applied just before union starts and then is left on about 10 days.

surfaces and some thickness and as a direct covering for cartilage and bone, a skin flap has no competition.

As Pickerill pointed out more than two decades ago, it is necessary that there should be adequate buccal and labial sulci so that both jaws, lips, tongue, and cheeks can perform their natural and proper functions of both mastication and speech. It is also necessary that adequate sulci should be formed in order that artificial dentures may be worn. For intra-oral contractures in the sulci, particularly, the method of applying an outlay stent skin graft as devised by Waldron and Pickerill has distinct advantages.

FRACTURE DEFORMITIES OF THE BONE

To correct late severe injuries of the bony framework of the face and jaws successfully, one must understand the essential nature of the original lesion. Probably if the matter is discussed in a regional fashion, more clarity will be offered.

Forehead. When a healed symptomless depression of the frontal bone, a bony loss of the supra-orbital ridge (Fig. 7, a and b), or an actual loss of substance of the frontal bone is present, as a rule, the easiest and best correction is given when the superimposed skin flaps are turned back and a properly bevelled and fitted autogenous cartilaginous inlay graft is "stepped" in the edges of the defect and held by some type of fixing suture. One should not attempt such a reconstruction until at least 6 months have elapsed after any evidence of infection. For a circular loss of substance of the frontal bone, McIndoe has been most satisfied with a bone plate taken from the inner aspect of the iliac bone. He points out that the natural configuration of this plate is that of the forehead.

Nasal bones. Two distinct types of late nasal bone fractures are seen, the uncorrected

a b c

Fig. 10. This girl sustained a crushing fracture of her nasal—lacrimal, ethmoidal, and bilateral anterior maxillary—bones. a, Shows anterior view of result before corrective measures were taken. A right angled autogenous cartilage was inserted over a dorsal piece of cartilage to elevate its bridge, raise the tip, and narrow the base of the nose. b, Front view after completion of operation. c, Lateral view, after operation.

Fig. 11. a, left. Crushing compound fracture of the nose. Repaired by inserting 2 superimposed pieces of cartilage at two different operations. The second one was a right angled cartilage. b, Result after operation.

lateral fracture due to a lateral blow and the old telescoping fracture due to crushing frontal blow.

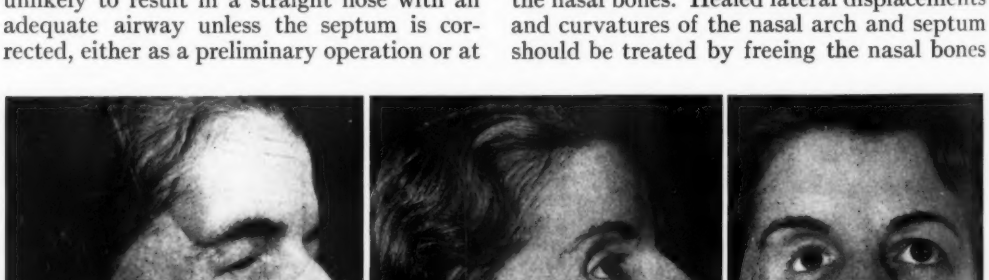
Unless the insertion of cartilage or bone will be necessary for correction, fracture deformities of the nasal bones should be attacked as soon as possible. Within 3 weeks, manipulation is often successful. As time passes, the tendency is for the septal cartilaginous and bony partition, as well as the bony structures of the arch, to become fixed in a distorted position. The septal cartilage may liquefy. Secondary changes tend to occur in the alæ and lateral cartilages which may prevent correction even when the mobilization and disimpaction of the bones have been thorough. Thus, the problem of correction is complicated after firm consolidation has occurred by the

a b c

Fig. 12. a, Roentgenogram showing malar lowered bone which is pushed backward and rotated. b, Head cast with projecting wire to which a wire passed through malar bone is attached. *A* indicates the wire. c, Roentgenogram showing a fine steel wire has been passed through the malar bone to hold it in elevated position after disimpaction (*A*, fine steel wire) (*B*, heavy projecting wire in the head cast).

Fig. 13. a, left. This man had a compound fracture of the anterior maxilla and its malar bone. The malar bone was displaced backward and laid against the ramus of the jaw and the coronoid process of the mandible. He could not open his mouth. The displaced bone was removed. (*A*, conjunctiva.) The anterior cheek was lined with a flap from the neck. The external cheek was repaired by means of a skin flap from the forehead. A prosthesis was used to hold the cheek forward. b, A final operation to raise the orbit has been done after this photograph was taken but we have been unable to get the patient to return as yet for a final photograph.

fact that bony manipulation alone is most unlikely to result in a straight nose with an adequate airway unless the septum is corrected, either as a preliminary operation or at the time of mobilization and disimpaction of the nasal bones. Healed lateral displacements and curvatures of the nasal arch and septum should be treated by freeing the nasal bones



a b c

Fig. 14. a, Depressed contoural deformity of soft tissues and malar and anterior maxillary bones. The lesion was camouflaged by inserting a fairly large properly shaped cartilage graft subcutaneously anterior to the malar and maxillary bone and artificial eye. b, Final result several months later, lateral view. c, Front view afterward.

Fig. 15. a, left. Fracture of anterior maxilla resulting in lowering of the eye globe. The eyelid cannot be opened because of a conjunctival symblepharon. A cartilage graft was inserted subperiosteally above the lowered supraorbital plate to elevate the eyeball and to round out the face anteriorly. b, Final result several months later. A plastic operation was done on the conjunctiva to alleviate the symblepharon. The symblepharon was not entirely alleviated. Since this photograph was taken a skin graft has been inserted into the upper sulcus of the conjunctival sac to free the sulcus contracture which limited the movement of the upper eyelid.

from the maxillary processes with either the chisel or a saw (Fig. 8, a and b). In the more severe types comminution of the nasal bones should be radical. Whenever necessary, the nasal septum should be treated by judicious cartilaginous section or submucous resection. In certain instances it is advisable to free the septum at the nasal spine. When one side of the nasal arch is too long, a wedge of bone should be removed from the base of the longer side. As a rule, when the disimpaction and mobilization is thorough, there is so slight a tendency for the nose to return to its former position that it can be kept in position by means of one of the many simple external nasal splints commonly used after rhinoplastic operations. When one of these splints is insufficient, sometimes a through-and-through fine steel wire may be utilized to hook over a dental roll or rubber tube on the side to which the deviation tends and over a cuspid or bicuspid tooth on the opposite side. At other times, it may be wiser to apply definite lateral immobilization by means of a head cast from which projects a double heavy wire which lies along the lateral side of the nose. Beneath the wire is placed a felt pad (Fig. 9).

Generally, it will be found to be a useless gesture if one attempts to reduce a late telescoping fracture of the nasal bones. If the base is too markedly broadened and splayed, it may be wise to narrow the base previously to rebuilding the bridge by sectioning the nasal arch at the maxillary attachments after sectioning the nasal arch in the midline. The septal deformity also should be alleviated at this time. The real mandate in addition to provision for a free airway for the correction of healed crushing fractures of the nose is elevation of the bridge or bridge and tip by the insertion of an appropriate autogenous transplant of cartilage or bone and cartilage. When the tip is depressed, and the alar base broad, a right angled piece of cartilage, the lower end of which impinges on the anterior maxilla in the region of the spine after it has been rongeured away, is indicated (Fig. 10, a, b, c). Not uncommonly, the insertion of two thicknesses of cartilage are necessary to gain a bridge of the proper elevation (Fig. 11). Whether or not both of the cartilages are inserted at one sitting will depend upon the degree of mobilization of the soft tissue possible to obtain.

If a septal operation is required, it may be done either at least 2 months previous to the cartilage transplant or postponed until after the cartilage transplant has had sufficient time to be thoroughly acclimated to its new bed.

Fig. 16. This man had sustained a compound crushing fracture of his anterior maxilla. The eye globe was not lowered much but the lower eyelid was pulled slightly downward. The defect was principally a contoural one. Skin flaps were turned backward. A properly fitted piece of autogenous cartilage was inserted. a, Front view before operation. b, Lateral view before operation. c, Front view after operation. d, Lateral view after operation.

Malar zygomatic compound. The malar bone is characterized by a central thick heavy bone standing on four weaker bony supports—frontal, orbital, maxillary, and zygomatic. Blows from different angles produce considerable variation in fracture lines. Most often, the bone is displaced inward, downward, and backward, and is likely to be somewhat rotated. As a general rule, there is comminution of the maxilla which often results in destruction or depression of the infra-orbital plate which if uncorrected results in downward displacement of the globe of the eye with diplopia. The first decision the surgeon is called upon to make is whether treatment is to begin with an effort at disimpaction and elevation of the malar maxillary displacement or whether treatment by camouflage is advisable by superimposing some filling material such as derma, temporal muscle (Gillies), or cartilage above the bone beneath the skin and subcutaneous tissues. Usually, if displacement is severe, some camouflage treatment will eventually be necessary even if fair reposition is obtained.

a

b

c

Fig. 17. a, Wire passed around the mental region of the mandible because of a bilateral fracture of the body. Jaw edentulous. Wire passes through palate, over maxillary nasal surface, and beneath the lip. b, Head cast with heavy projecting wire to which is attached a fine steel wire passed through the mental region of the mandible. This woman had a bilateral malunion with open bite of long duration. Simple interdental wiring of the teeth was insufficient to maintain occlusion. c, Pulley traction after old bilateral malunion of the body of the mandible to stretch the geniohyoid muscles. This is sometimes necessary.

After union has become firm, replacement by means of leverage without dividing the points of union is as a rule unsuccessful. Successful efforts at replacement will largely depend upon accurate diagnosis of the position of the fracture lines, and the type of fixation used to hold the bone in position after disimpaction and repositioning.

For disimpaction, a double approach is as a rule necessary: (1) from beneath the upper lip across the anterior maxillary wall and (2) through an incision in the upper temporal

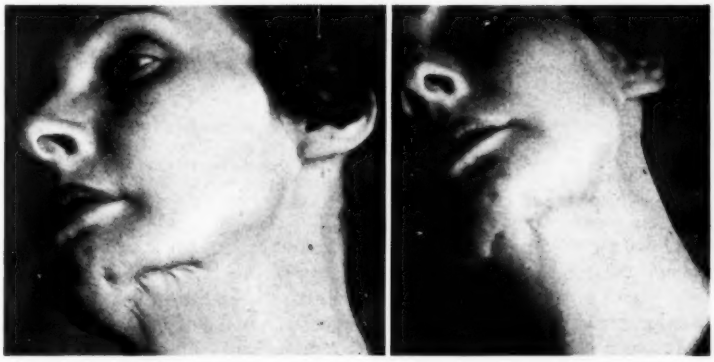


Fig. 18. a, left. External parallel loss of bone causing a contoural deformity. Corrected by the insertion of an autogenous cartilage graft. b, Result several months later.

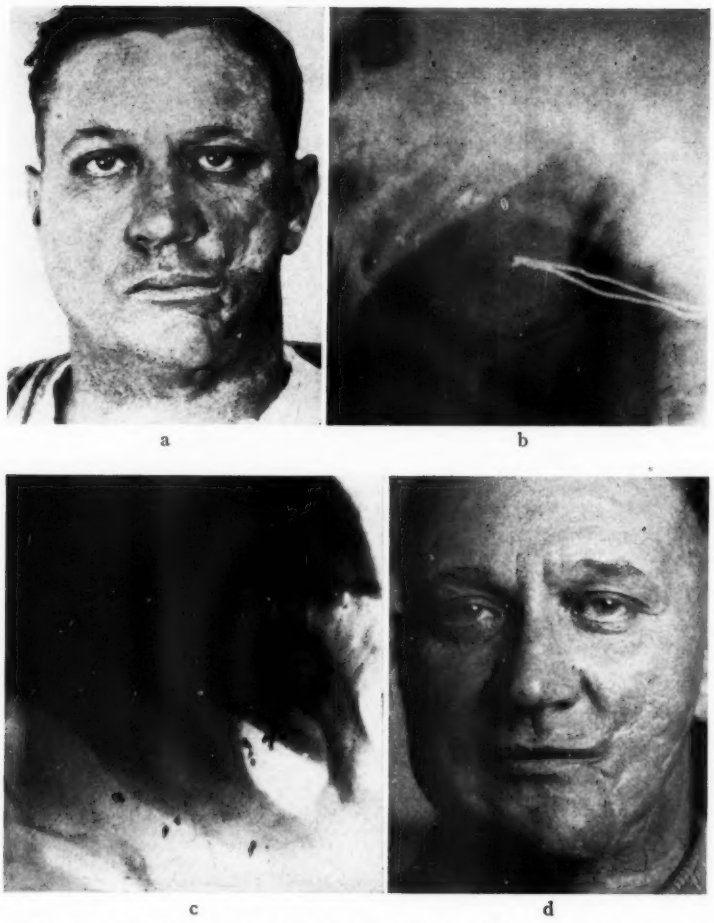


Fig. 19. a, Patient in whom about 4 inches of the mandible was lost because of a gunshot wound. b, Roentgenogram showing the bony defect. The ramus of the jaw had been pulled upward and forward. A wire has been placed through the ramus to pull it backward. c, Roentgenogram about 1 year after a piece of the seventh rib had been transplanted into the bony defect. d, Patient's appearance after the bone graft had become solid and firm. Prior to the placing of the bone graft, we had prepared an adequate internal and external lining so there would be no difficulty in getting a good soft tissue bed for the bone graft. This photograph shows external lining which was laid in from a flap from the neck. The internal lining was made from a flap turned up from the neck.

region so that a chisel may be passed posteriorly to the temporal muscle to a point behind the malar bone. These approaches also allow one to pry the bone forward.

In several cases, the bone has been repositioned, and held in position by means of a fine steel wire which is passed through the bone and attached to a projecting heavy wire laid in a plaster head cast (Fig. 12, a, b, c).

In one individual in whom the malar bone was pushed very markedly medially and posteriorly in such a fashion that it impinged upon the coronoid process and ramus preventing the man from opening his mouth, the bone

was removed as reposition seemed hopeless (Fig. 13, a and b). An intra-oral prosthesis was used to support the soft tissues of the anterior cheek after appropriate reparative surgery had been completed.

In the majority of individuals with a depressed malar fracture, the most conservative and most successful result is given when the lesion is camouflaged. The insertion of a cartilage transplant of the proper size and shape gives a fairly satisfactory result as a general rule (Fig. 14, a, b, c). For a minor depression, the insertion of a dermal graft may be sufficient to give correction. When the infra-orbital plate is lowered, the insertion of a cartilage graft subperiosteally just above the lowered floor of the orbit may successfully raise the globe, but an entire correction of the diplopia is unusual (Fig. 15, a and b). Attempts to correct the enophthalmus by means of inserting cartilage posterior to the eyeball after making a Killian approach have been attempted, but without any noteworthy success.

Anterior maxilla and nasal ethmoidal lacrimal maxillary fracture deformities. As a rule, fractures of the alveolus and supra-structure of the maxilla, unless they are of the pulverizing, crushing type, do not call for late reconstruction. In the type of fracture which follows a severe head-on crash with the force falling at the level of the eye globes or slightly below, in addition to a nasal fracture, there results a telescoping of the ethmoidal and anterior maxillary wall compound as has been mentioned previously, when severe malar bone dislocation occurs. There is the same tendency for the infra-orbital plate to be displaced with a subsidence of the eye globe (Fig. 15, a and b) in anterior maxillary and nasal ethmoidal lacrimal maxillary crushing fractures. In addition, in nasal ethmoidal lacrimal maxillary fractures, the inner part of the orbital rim is crushed laterally in the orbit so that the eye globe tends to be pushed outward.

Healed depressions of the anterior maxillary wall when rather pronounced (Fig. 16, a, b, c, d) may be corrected by filling the depression with cartilage and, similarly, if the infra-orbital plate is lowered, the globe of the eye may be elevated by the subperiosteal insertion of cartilage above the lowered plate (Fig. 15, a and b).

The well known "dish-face" deformity caused by a healed nasal ethmoidal maxillary fracture displacement is difficult to correct. Satisfactory elevation of the impaction is hardly possible, but there are several procedures of the camouflage nature which may give quite remarkable improvement both in appearance and function (Fig. 10, a, b, c). McIndoe states that sometimes, before 6 weeks have passed, this impaction may be advanced as much as ½ inch by means of pulley traction. Often, the tear ducts become blocked. By removal of the intervening bony partition and appropriate plastic operation, the tear sac may be drained into the nose. When the splayed inner margin of the orbit is encroaching upon the orbit at its medial rim, the frontal process of the maxilla and the lacrimal ridge should be rongeured away.

Fracture deformities of the mandible. Fracture deformities of the mandible may be divided roughly into two types: those due to malunion, and those due to loss of bone.

Malunion of the body of the mandible is best corrected by maintaining the fragments in position after sawing across the line of fracture with a Gigli saw. There is more of a tendency for non-union to occur after this procedure than there is following the original fracture.

Occasionally, one sees a bilateral fracture of the mandible which has united in open bite position. The body in this case will need to be severed bilaterally. One may experience difficulty in holding the anterior fragment in its proper position by simply wiring the anterior teeth together. Three procedures in such a situation may overcome the difficulty: (1) a circumferential wire may be passed in the midline about the body of the mandible through a palate drill hole thence over the bony floor of the nostril and beneath the upper lip (Fig. 17, 1); (2) a head cast with a long heavy springy projecting wire may be attached to a small steel wire passed through a drill hole in the lower mental projection of the fragment in the midline (Fig. 17, b); and (3) in old and marked malunion, the muscles may have to be stretched by pulley traction (Fig. 17, c).

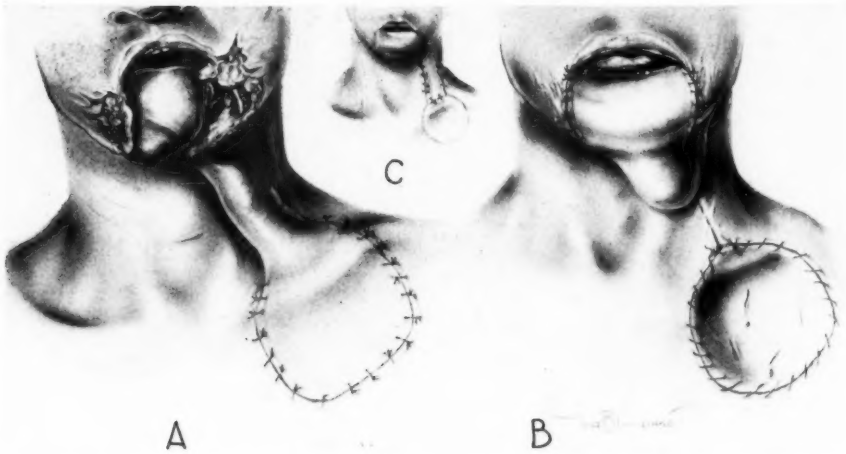


Fig. 20. a, Flap over the clavicle has been outlined. The clavicle has been split longitudinally so that one-half of the clavicle lies in the flap. The flap has been tubed. The lower end of it has been sewed back in place as a delayed flap. b, About 2 weeks later the flap including the bony segment of the clavicle is thrown up into the defect in the chin and the distal end of the flap is used to throw anterior to the tongue to re-form the interior lining of the lower lip. c, After about 3 weeks the pedicle of the flap is cut and sewed back into place. The pedicle of the tubed flap is laid back onto the neck and the granulating area is covered with a Thiersch graft.

Occasionally, an old fracture dislocation of the condyle is encountered in which the chin has fallen to one side, and backward, or if bilateral, the chin may be retrusive, and open bite is present. This condition may be corrected by cross section of the mandible so that

Fig. 21. a, left. Gunshot wound of the lower jaw in which a section of the mandible was completely destroyed. This case was repaired by a pedicled flap in which was embedded a bone graft from the clavicle. b, Result 2 weeks after operation.

a b c

Fig. 22. a, Gunshot wound of the mental region which blew away the mental part of the mandible but a fair amount of the tissues of the lower lip and chin remained. In this case a sliding bone graft from the longer side of the mandible was used to throw a piece of bone across the mental region. The lower edge of the mandible was used and the skin of the cheek was left attached to it. Dotted line shows the line of section of the mandible in the long side of the jaw. b, Lower edge of the mandible thrown across to the short side and wired in place. The patient obtained good union of the mandible. Later a cartilage graft along the lower edge of the jaw from which the sliding bone graft was cut was used to fill in the contoural defect. c, Final result. Defect on short side filled in. The lower lip is a little tight. Front view was nearly normal.

the sectioned bone will interlock when the chin is drawn forward and the open bite corrected by approximation of the anterior teeth (Fig. 17, c).

Open bite occurs if a complete supra-structural fracture of the maxilla is allowed to unite in a position lower than normal. Bilateral section of the body of the mandible anterior to the first impinging molar will allow one to obtain anterior occlusion of the teeth.

Parallel loss of mandibular bone along the lower border causes a contoural defect which may be corrected by the implantation of cartilage (Fig. 18, a and b). As a rule, intra-oral loss is compensated for by prosthesis.

Loss of continuity of the mandible is always associated with considerable dysfunction because the muscles of mastication tend to lose their normal co-ordinated activity. The scar tissue adds to the dysfunction.

When the loss of continuity is not greater than a few centimeters, the method of Delagénière or Kazanjian of placing multiple small pieces of bone and periosteum across the defect may be quite applicable. During the last war, of 38 patients operated upon by this method in the United States Army, 27, or 71 per cent, were successful.

Defects in the lower jaw region complicated by a fairly large loss in bony continuity may be repaired in 4 different ways: (1) by free bone graft; (2) by bone transplanted in a pedicled flap from a distance; (3) by sliding a section of bone from a neighboring fragment without freeing it from its soft tissue attachments; and (4) by the substitution of prosthesis for the loss of about one-half of the mandible.

A free bone graft is most applicable when the surrounding soft tissues are sufficient or easily transferred and when the defect is a long one of the body or the body and a part of the ramus of the mandible. The graft may be taken from a rib or the crest of the ilium. The crest of the ilium is preferable when the angle is absent (Fig. 19, a, b, c, d).

Sometimes, time can be saved when it is necessary to add soft tissue lining and covering as well as structural support if all three (lining, covering, and structural support) are transplanted together. A fairly accessible area to obtain the bone and necessary soft tissue is the clavicular area. A split half of a longitudinal section of the clavicle is buried in a skin flap doubled upon itself (Fig. 20, a, b and 21, a and b).

When the body of the mandible is long on one side, and there is also a soft tissue defect, and especially if the loss is in the mental region, an oblique longitudinal segment of the lower part of the long body fragment with soft tissue attachment may be slipped across to bridge the bony defect. Later, after union is obtained, the contour of the face may be improved if the soft tissues are rearranged and replaced to nearly their former position (Fig. 22, a, b, c).

If the whole region of the position of the half mandible that has been lost is lined with a skin flap, it is possible to hold the intact half of the jaw in fair position and to bolster out the contour of the cheek on the defective side by the use of an intra-oral prosthesis in lieu of the lost half of the mandible.

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THE IMMEDIATE AND LATE TREATMENT OF INJURIES ABOUT THE ORBIT

Presentation with Case Reports

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IN the treatment of traumatisms to and about the orbit, it is necessary to consider not only the early or immediate treatment but also the late treatment. In many instances, late deformities and disfigurements are due to improper and inadequate treatment early in the condition. One might even say that the immediate posttraumatic treatment modifies to a tremendous extent the later condition which can develop. This is true not only in the consideration of defects of the soft tissues but of bone injuries as well.

First, in the immediate treatment of gunshot wounds of the orbit, especially in those patients who will certainly recover, early enucleation, if the eyeball seems to be lost beyond repair, is necessary. A careful débridement should be done with the removal of foreign bodies. It is not at all uncommon that the fluoroscope is required, and at most times it is an aid in this procedure. At times, large fragments and large foreign bodies are so situated that it might be unwise to remove them. When that occurs, the patient should be kept under careful observation, and the surgeon be prepared at all times to reoperate, if necessary. Bone fragments which are completely detached had best be removed. Those still adherent to the periosteum, and by this to the uninjured portion of the orbit, may be spared. Completely detached fragments, however, will not heal in position properly; usually they form a sequestrum and later demand removal. Figure 1 is such an encapsulated sequestrum. Antitetanic serum is necessary, and usually drainage. Figure 2 is the roentgenogram of a large foreign body, so called "punkin ball," which entered the lateral side of the orbit, traversed it, and lodged in the medial wall of the orbit. The eye had to be enucleated, but the foreign body has been permitted to remain in place now for almost 5 years, without any symptoms whatsoever.

The matter of intra-ocular foreign bodies has been omitted deliberately from this presentation. This is a subject complete within itself. Many cases of orbital injuries have accompanying neurological conditions, as would be expected. The graver such complications, the less likely it is that the patient will recover. To repeat, débridement, enucleation, the removal of detached fragments and of foreign bodies, and the administration of antitetanic serum are the important factors connected with these conditions. Penetrating or stab wounds without orbital wall complications should be treated with a pressure bandage and with antitetanic serum also.

Fractures of the orbit. Fractures of the roof of the orbit are rather likely neurosurgical problems and are seldom, if ever, simple. The same applies to fractures of the inner wall of the orbit. These usually have not only neurosurgical, but also rhinological conditions complicating them. Fractures of the outer wall of the orbit, when simple, are usually reducible by pressure with a stout periosteal elevator applied against the bone from the conjunctival surface at the outer canthal angle. When they are impacted, an incision may be made here and reduction can be achieved in this manner. Usually, however, such injuries must be reduced otherwise. An incision is to be made above the zygoma and through the temporal fossa. A stout periosteal elevator is introduced through that down across the temporal fossa to rest against the fractured portion of the rim of the orbit. Pressure applied there and augmented, as is necessary, by external manipulations, should reduce almost any fracture with adequate alinement. It is quite possible that a fracture here would be so extensive that one must incise, reduce the fracture through the open incision, and then suture the fragments in position, the edges of the torn periosteum being utilized for the introduction of stout catgut sutures. It is seldom if ever necessary to use silver wire sutures. Figures 3 and 4 are roentgenograms of a fractured outer angle of the orbit which was reduced without incision by pressure applied against the fragment through the conjunctival surface of the external canthal angle.

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Fig. 1. Roentgenogram of encapsulated sequestrum of rim of orbit.

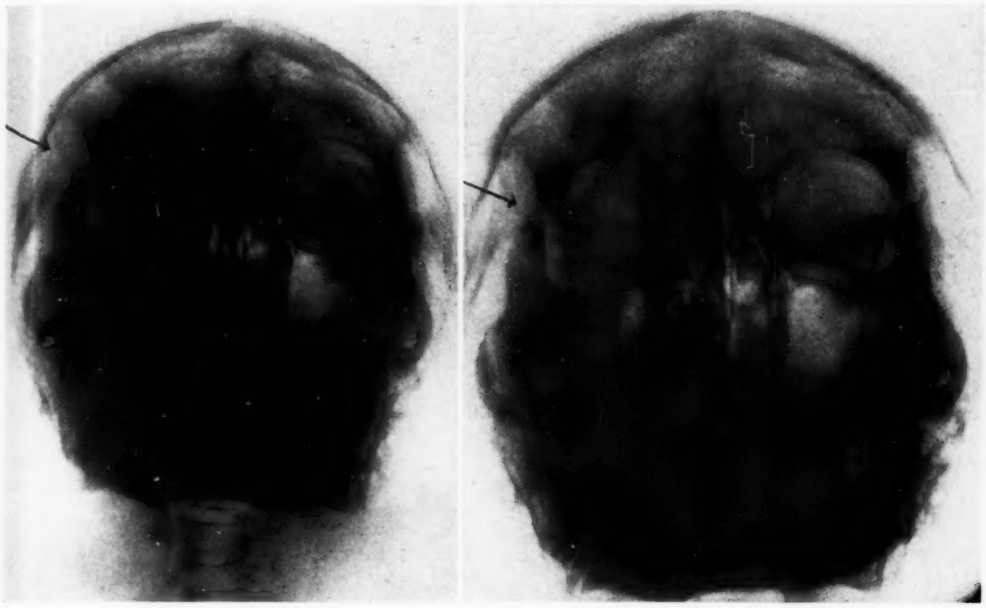
Fig. 2. Roentgenogram of large foreign body firmly adherent to medial wall of orbit.

Fractures of the floor of the orbit are perhaps the most neglected of all in so far as this primary treatment is concerned. A stout periosteal elevator can be passed into the semilunar fossa, through an incision if necessary from the mouth and with pressure applied against the rim of the orbit; marked improvement was obtained thereby, even to complete alinement. In some instances, it is perfectly proper to open the maxillary sinus and to reduce the fracture through that sinusotomy. When this is used, the floor of the orbit can be splinted temporarily by fitting a molded portion of dental stent within the maxillary sinus to support it. The late effects of an unreduced fracture of the floor of the orbit are so serious that every effort should be made to correct them at the time of the accident, if it is at all possible.

Fractures of the orbit which have healed in deformity should not be rebroken. Exostoses and displaced but solidified fragments overriding and causing either a deformity or an impairment of ocular motility should be removed through a clean surgical incision. A depressed eyeball from an old fracture of the floor of the orbit—probably the most common deformity—should be corrected by a costal cartilage graft. A piece sufficiently thick to raise the eyeball to the proper level is removed, the periosteum on the rim of the orbit is incised and elevated, and this cartilage graft of proper shape and thickness slipped beneath the periosteum. If the periosteum itself cannot then be closed by sutures, an adherent cicatrix will occur, which, after complete healing, must be resected, to obviate a permanent crescentic adherent depressed scar in the soft tissue there. Figures 5 to 8 are illustrations of a cartilage graft correction of a posttraumatic depressed floor and damaged rim of the orbit, the correction being finally completed with a pedicle flap.

Many of these patients will need additional muscle surgery. This is not an especially difficult matter, however, compared with the surgery necessary for elevating the depressed eyeball. Figures 9 and 10 are the illustrations of a simple depressed orbital floor, corrected with a scale of cartilage. The horizontal lines show at a glance the amount of elevation obtained. In Figure 10, the lower lid on the right shows the minimum scarring possible.

In regard to injuries of the globe, it is necessary to consider the globe itself and its extra-ocular muscles separately.



Figs. 3 and 4. Roentgenograms of case before and after reduction of orbital fractures.

A small proportion of cases present themselves with injuries which are without doubt hopeless from a reparative standpoint. Such instances as a massive laceration of the sclera with loss of the vitreous, and the prolapse of the uvea, if they appear early, should have an immediate enucleation. If, however, there has been an interval of more than 2 days after the injury, ablation of the cornea and an evisceration of the scleral shell is the better procedure. Meningeal infection has

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 5. Loss of rim of orbit and the major portion of the floor of the orbit.
Fig. 6. Immediately after the cartilage graft.

Fig. 7. Pedicle flap in place.
Fig. 8. Pedicle of flap returned; correction has been completed.

Figs. 9 and 10. Illustrations before and after a similar surgical correction.

Fig. 11. Markedly traumatized eye demanding enucleation.

occurred, though infrequently, following the enucleation of an infected contused eyeball. Figure 11 is a markedly traumatized eye fit only for enucleation, Figures 12 and 13 illustrate the primary suturing terraced and with tarsal plate and conjunctival suture lines offset from the skin suture lines minimizing these by later notching of the lid margins.

A word here as to sympathetic ophthalmia is especially relevant. This complication can occur in the absence of an open wound; it was seen rather recently in a case of equatorial subconjunctival rupture of the globe from a direct blow. The opposite extreme is also seen. Massive limbic lacerations, when handled adequately, frequently recover, even though the injury has been in the so called danger zone. It is rather likely that a chronic irritative condition of the ciliary body or other portions of the uveal tract, following trauma, is absolutely necessary for the development of sympathetic ophthalmia regardless of whether the condition is caused by tissue sensitivity or by bacterial etiology.

In a case of limbic laceration without iris or ciliary body incarceration; if this can be closed surgically, the likelihood of sympathetic ophthalmia is not imminent. Prolapse of any portion of the uvea must be corrected. In these, the surgical judgment as to whether or not to enucleate is perhaps the most important factor in the treatment. No one wishes to be responsible for the development of sympathetic ophthalmia. At the same time, the opportunity to save an eye with usable vision, if utilized with success, is a far greater achievement than the most beautifully performed enucleation. Prophylaxis in every sense is the most serious consideration in regard to the development of this condition.

Figs. 12 and 13. Illustrations of the primary suture terraced to prevent notching of the lid margin.

The relevant factors in deciding for or against an enucleation can be reviewed. They are given in the order of severity; hence, naturally, are also a chart of ascending imperative indications. (1) The size and the shape of the laceration, i.e., the major portion of the laceration being anterior to the ora, posterior to the ora, at the ora, or from the ora extending anteriorly into the cornea; (2) prolapse of the uvea, and the severity of this; (3) the degree of intra-ocular hemorrhage present; (4) the amount of vitreous lost; (5) spontaneous extrusion of lens; (6) collapse of the globe; and (7) an immediately sightless eye—this is seldom, if ever, to be retained. Further modifying factors are as follows: an iris prolapse must be resected; in closure of a scleral wound the ciliary body cannot be pinched therein. Scleral wounds should be sutured. It is not sufficient to cover them with a conjunctival flap and hope that this will adequately bridge the defect. Black paraffinized sutures of 6-0 silk can be passed through the conjunctiva superficially, then through the two scleral lips of the wound, and out again through the conjunctiva so that these can be removed readily following healing. After sufficient of these have been introduced and tied, the conjunctival

a b c

Fig. 14. a, Partial ptosis from incomplete sectioning of levator. b, Ptosis corrected by a reattachment of the levator. c, Same case to show the normal degree of lid closure possible after the correction.

wound may be closed itself, so that this suture line is well offset from the scleral suture line. It may even be necessary and perhaps wise to use a sliding conjunctival flap. Any wound which passes into the cornea must be closed with such a flap. It is necessary to seal off the anterior chamber early and thus prevent synechiae, not only at the angle, but also anterior and posterior synechiae. The late correction of a descemetocele is a difficult procedure compared to its prevention by the use of such a flap. This applies especially to punctate acid burns of the cornea. As said before, any degree of iris prolapse must be corrected by a surgical iridectomy. Alkali burns of the conjunctiva and the cornea, if severe, usually damage the eye to such an extent that vision is seriously endangered. The symblepharon which develops means later correction with mucous membrane. The use of neutral ammonium tartrate will minimize this damage more than any other form of treatment. In several instances, when, following débridement, mucous membrane grafts were used very early in the course of the treatment, the end-results seemed to be unusually good.

Scleral wounds which pass toward the equator beyond the ora should be rimmed along both lips of the wound with diathermy pin punctures, in the hope that thereby a later retinal separation may be presented.

The surgery of cyclodialysis, the uneventful correction of limbic ectasia, even the surgery of retinal separation, illustrate the resistance to surgical trauma which the uveal tract possesses. On the other hand, the indiscreet application of the cautery for a small postcataract extraction iris prolapse has been sufficient to precipitate sympathetic ophthalmia. It seems that the threshold

Fig. 15. Utilization of occipitofrontalis for complete posttraumatic ptosis.

Fig. 16. Mechanical ptosis from an adherent cicatrix.

between proper and nonpermissible surgical procedures to the uvea is not very wide when chronic irritation is an additional factor.

The therapy of anterior dislocation of the lens into the anterior chamber is upon a sound basis and needs no mention here. The differential diagnosis between this and bloodstaining of the cornea should never be in doubt. Subconjunctival dislocation of the lens through a limbic scleral laceration is a rather serious condition. Posterior dislocation of the lens from contusion and compression injuries is also a surgical problem, but it is not as outstanding an emergency situation as is that of an anterior dislocation.

Another point relevant here, though more important from a prognostic standpoint, is the remarkable number of contusion and compression injuries with massive vitreous hemorrhages. It has seemed that repeated anterior chamber paracentesis combined with subconjunctival injections of a mildly hypertonic salt solution increases, to a great degree, the rate of absorption of these vitreous hemorrhages. In posterior scleral injuries which involve the optic nerve with a resulting secondary optic nerve atrophy, one should be doubly certain that there is no deep orbital bone involvement. In one such case, the diagnosis of such a complication was not made until autopsy, following death from a suppurative meningitis. The presence of this complication may mean a radical change in the immediate posttraumatic treatment of the patient. Ophthalmologically, it has the same relationship to prognosis as a posttraumatic rhinorrhea has to rhinology.

In regard to traumatisms of the ocular muscles, the immediate primary treatment is negligible as compared, in importance, to the later treatment. It is very certain that one would not operate upon a ptosis until complete healing had occurred after an injury. The same applies to the other ocular muscles. Contusion sixth nerve paralysis, seen rather commonly (as in football injuries) and due, rather probably, to retrobulbar hemorrhage, certainly should have nothing except the most conservative treatment. Probable lacerations of the ocular muscles from a perforating wound, as from a sled runner or the end of an iron picket, should have as the immediate treatment only drainage from the depths of the orbit with rubber tissue, and perhaps compresses with hot 10 per cent magnesium sulphate solution. Injuries to the lids themselves in such instances should be sutured primarily, but not the extra-ocular muscles (Fig. 11). If the nerve supply to these is destroyed then the surgery would be of no avail; and if still intact, later surgery may not be necessary. At all events, one can proceed later with deliberately planned constructive surgery. The correction of the diplopia will then be achieved according to well established principles.

Ptosis may be due to the partial sectioning of the levator with its nerve supply still intact. These instances will oftentimes show after the primary healing a bit of normal lid elevation, usually at the inner angle. In such instances, the

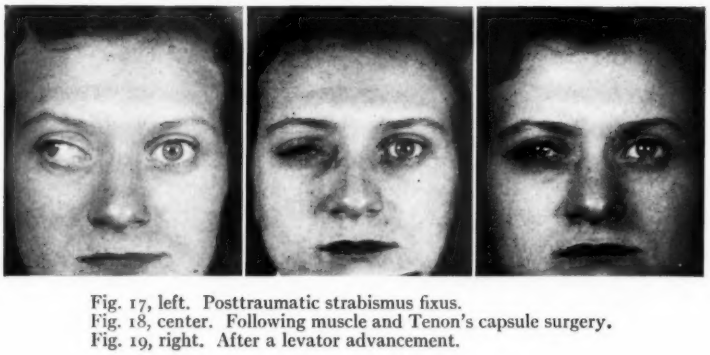


Fig. 17, left. Posttraumatic strabismus fixus.
Fig. 18, center. Following muscle and Tenon's capsule surgery.
Fig. 19, right. After a levator advancement.

Fig. 20. Wiener's suggestion for lid closure as seen in upper lid.

Fig. 21, left. Notching of upper and lower lid before correction.
Fig. 22. After correction.

surgery is relatively simple. The dissection should release the retracted levator for adequate reattachment to the tarsal plate. Figure 14 shows such a case; the incomplete sectioning of the levator was corrected by this type of reattachment. a is the original defect, b the correction, c the closure possible following correction. In the case of a completely destroyed levator, the ptosis surgery planned should be based upon the utilization of the occipitofrontalis, as in Figure 15. Ptosis from superficial and deep lid cicatrices (Fig. 16) to be discussed under the injuries of the lids is a matter wholly of scar resection and resuture.

The later surgery of posttraumatic ocular motor injuries is a bit more difficult, or perhaps more complicated, than the other ocular motor paralyses, nontraumatic in etiology. The former patients will often have Tenon's capsule incarcerated into scleral cicatrices. Mild to severe degrees of strabismus fixus are seen. The elevators are not at all uncommonly paralyzed, are adherent with and to the lids by the scar, and naturally with high degrees of hypertropia. An intact superior oblique muscle can oftentimes be utilized to replace a completely paralyzed internal rectus. Tendon transplants from normal superior and inferior recti are of greatest assistance in the surgical correction of a traumatic external rectus paralysis. They are indicated, however, only when the eye cannot be externally rotated to the midline of the palpebral fissure. Divergent strabismus fixus, especially when accompanied by some exophthalmos and ptosis, can occasionally be rather well held in a primary position by a brutal tenotomy of the external rectus and incision of Tenon's capsule, carried up and down to the edges of the superior and inferior recti and combined with muscle and capsule advancement of the internal rectus. The operation is completed by the application of the suggestion of Reese, occasionally necessary following an orbitotomy (Fig. 17), in which buried nonabsorbable sutures are passed from the septum orbitale through Tenon's capsule to the edge of the periosteum at the lower rim of the orbit and back similarly, and there tied. In such instances, a Hess, a Hunt-Tansley, or a fascial sling operation should be considered for the correction of the ptosis. Figure 17 shows a case of posttraumatic strabismus fixus, corrected, as in Figure 18, with muscle and Tenon's capsule surgery, and Figure

Fig. 23. Sketch to illustrate the suture line used.

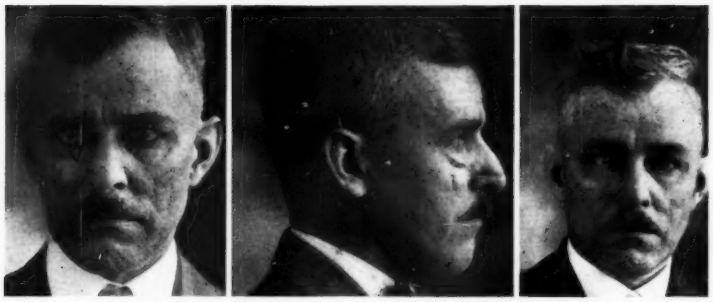


Fig. 24, left. Front view of a marked lid defect.
Fig. 25, center. Side view of a marked lid defect.
Fig. 27, right. End-result.

19, after a levator advancement. Cases of high degree posttraumatic ocular motor palsies may be so severe, when accompanied, as they so often are, by extensive choroidal and retinal lacerations and blindness, that, for purely cosmetic reasons, they are best treated by an enucleation with an implant into Tenon's capsule. Later in treating the elevator paralyses, one should not forget the benefit which can be obtained from tenotomizing the contralateral inferior oblique. Also, it is rather likely that an advancement of a paretic muscle should always be combined with the recession of the same sided antagonist.

In treating or handling traumatisms of the lids, the primary surgery is of outstanding importance; this applies especially to such injuries as lacerations at the outer canthal angle, through-and-through tears of the lids, and windshield cuts at the internal canthal angle, running up into the upper and/or down into the lower lid. In soft tissue accidents wherein one is certain that soft tissue has been lost, as a result of the accident, the primary suturing may utilize a very moderate amount of the principles of sliding flaps. In these cases, though, it is certain that secondary and later surgery will be necessary. Free skin grafts and pedicle flaps should not be used in the primary surgery of any injury of the lid except under most extraordinary circumstances.

There is quite a bit of difference in handling the primary suturing of lid injuries which lie parallel to the lid margin, and those which are vertical or perpendicular to the lid margin. In both instances, they should be closed in layers. In the first instance, the conjunctiva is to be closed with buried 6-0 catgut, the levator in the upper lid and

a b c

Fig. 26. Sketches to show the scheme used to release the tissues and break up the pull of the scars.

Fig. 28.

Fig. 29.

Fig. 30.

Figs. 28, 29, and 30. Sketch for closure of inner angle windshield cut and re-establishment of canaliculus drainage.

Fig. 31.

Fig. 32.

Fig. 34.

Fig. 35.

Fig. 36.

Figs. 31 and 32. Lower lid inner angle defect resulting from razor fight.

Figs. 34 and 35. Front and side view immediately after operation to illustrate the exact carrying out of the suggested plan.

Fig. 36. At the time of the removal of the sutures. Some postoperative edema still present.

Fig. 33. Sketches of scar tissue resection planned before operation.

the orbicularis in both lids with 6-0 plain catgut, and the skin closed in accurate approximation with interrupted twisted black silk sutures. These last sutures need to be tied only lightly; approximation of the tissues is the important thing, not strangulation. Incisions and lacerations which are perpendicular to the lid margin may have their layers of sutures offset one from the other. The suture lines with injuries lying horizontal adjust themselves thus automatically and anatomically. The conjunctival and tarsal plates are to be sutured with buried 6-0 catgut sutures.

Fig. 37, left. Ectropion prior to correction. Notice the dense contraction cicatrix.

Fig. 38. Free skin graft correction of ectropion by the use of skin from the hairless skin behind the ear.

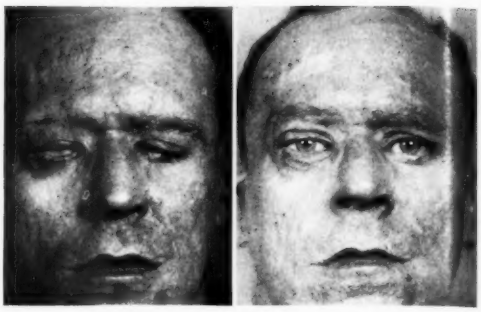


Fig. 39, left. Marked cicatricial thickening of lids with ectropion.

Fig. 40. After completion.

The orbicularis is then closed over this, if it is not too badly lacerated. The skin incision is to be offset toward the side with less intact skin surface, by resecting 2 or 3 millimeters of the skin along that lip of the lacerations and closing with interrupted sutures.

Notching at the lid margin in such lacerations can be prevented in several ways. Wiener's suggestion is to cut the lips of these wounds crescentically (see Fig. 20), the concavities facing each other. This tends to elongate the suture line, and thereby prevents notching. Two tiny tongues of lid margin tissue can be cut at the end of each lip of a laceration and then slivers of tissue from the sides of the incision are cut so that when a final marginal through-and-through suture is placed, these two tongues will mound up or pout out into redundancy. Excess there, following complete healing, can be wiped off readily with an application of the actual cautery. However, the more careful the approximation of all layers, especially at the lid margin, the less likely will any notching occur. If a vertical laceration can be closed in steps or terraces or inclined away from the perpendicular by tiny triangle resections, it will be of great assistance. Figures 21 and 22 show such an instance. Figure 23 is the drawing to demonstrate the closure. Figures 24 and 25 are front and side views of a marked lid defect with gross contraction cicatrices. Figure 26 shows the scheme used to release the tissues and to break up the pull of the scars. Figure 27 is the end-result.

Fig. 41. Wheeler technique correction of upper and lower lids.

External canthal angle lacerations, when the obliquity at the outer angle is downward, should be overcorrected at the time of the primary suturing. Suturing the fibers and the raphe of the orbicularis and reattaching the external canthal ligament to the periosteum will achieve this. Those which oblique upward, ordinarily, do not need this overcorrection. In closing lid and conjunctival lacerations, one must be careful not to bury the caruncle; otherwise an entropion may occur at the inner angle with constant epiphora.

When a lower canaliculus has been cut, a No. 1 probe should be threaded through the lower punctum, to emerge from the cut distal lip of the canaliculus. With the probe then as a handle, the cut lid can be placed at its exact anatomical position. The probe should then pass readily into the lacrimal sac. Sutures are to be placed on the anterior and posterior surfaces of the lid, and on the lid margin bridging the laceration, for accurate approximation even to the use, if necessary, of buried 6-0 plain catgut. The major portions of the external end of the probe may be cut off with wire cutters, the end bent away from the lid margin, and this probe permitted to remain in

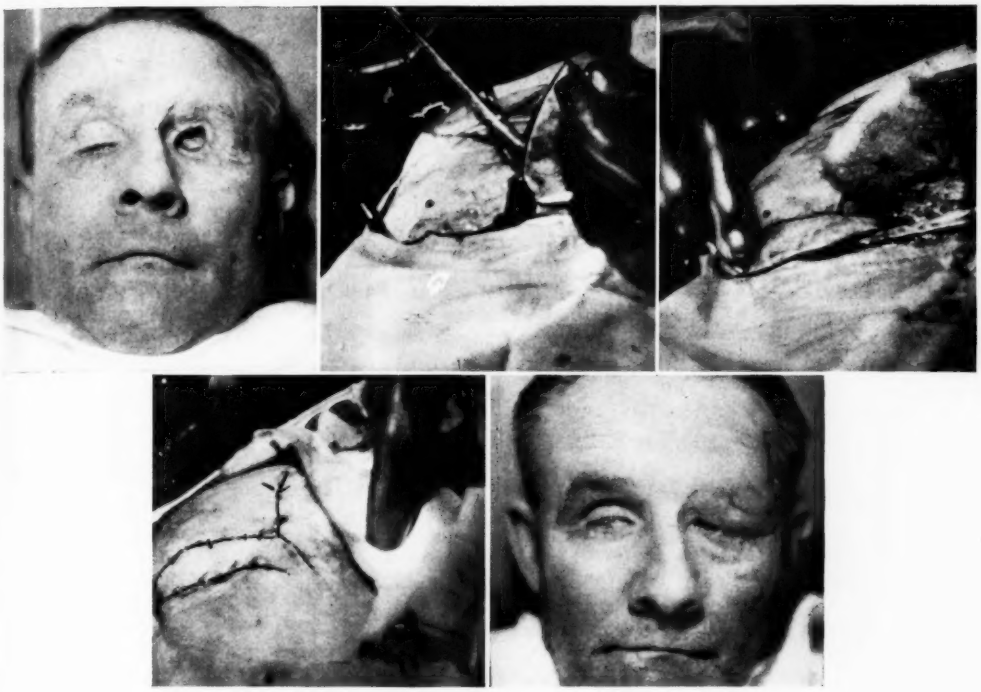


Fig. 42. The ideal utilization for a pedicle flap.

place for about 6 days. Later, some canaliculus probing will be necessary to prevent or correct a stricture. Figures 28, 29, and 30 show the technique and closure.

The later handling of lid traumatisms is to correct the deformities from contracting cicatrices or those defects due to the loss of soft tissue. Naturally, these latter will be more extensive and more difficult of repair. The first essential in any of these instances is to study the cases very carefully with photographs and from line sketches. In this way, the surgeon can decide the position of the necessary incisions and the scar resections and the positions and direction of subsequent sutures. He can estimate the amount of tissue which is lost, and how this is to be replaced. Figures 31 and 32 show the lower lid inner angle defects as a result of a razor fight. The sketches of Figures 33, a, b, and c, illustrate the scar tissue resection necessary to correct the defect as it was planned before operation. Figures 34 and 35 are front and side views of the patient made immediately after operation and illustrate the exactness with which the plan suggested could be carried out. Figure 36 is the same case at the time of the removal of the sutures. There is still some postoperative edema present as would be expected. The method of replacing the tissue depends upon the amount lost, the position of the defect, and the amount of scar tissue contamination in the surrounding tissues. There are several other less flexible requirements; for instance, a lost eyebrow should be replaced either by a temporal scalp flap or an occipital scalp free skin graft, and lid margins for cilia reconstruction should be replaced with a free full thickness graft from below the eyebrow.

Full thickness grafts of any type can be obtained from the upper lid on the opposite side, if this is still normal, or from that hairless portion of skin immediately behind the ear. Razor-cut grafts are readily obtained from the inside of the thigh, or, if Paget's dermatome is used, from the skin of the abdomen. The free skin graft cicatricial correction of ectropion, a condition in which lost epithelium must be replaced, is very satisfactorily corrected by any one of a number of procedures utilizing a free skin graft. Figures 37

Fig. 43. Fig. 44. Fig. 45. Fig. 46. Fig. 47.

Fig. 43. Loss of both upper and lower lid and of the eyeball.
Fig. 44. Correcting pedicle flap.
Fig. 45. The flap raised and attached to remains of lower lid.
Fig. 46. The flap attached to remains of upper lid.
Fig. 47. Pedicle resected, flap incised for palpebral fissure, patient wearing ocular prosthesis.

and 38 illustrate the correction of an ectropion by the use of a free skin graft from the hairless skin behind the ear. Figure 39 is a case of marked cicatricial thickening of all four lids with ectropion, with the loss of the major portion of the right eyebrow. Figure 40 shows the end-result following the use of Wheeler's technique. The intermarginal adhesions were sectioned, some time before, after they had been in place for 4 months. The case was completed with the scalp eyebrow graft as illustrated. Figure 41 shows a similar correction, more severe in degree, with the intermarginal adhesions still present, on the left, and in b, the end-result 6 months later.

Fig. 48. Two dissimilar cases for socket reconstruction.

Pedicle flaps (Fig. 42), if they are to be cut and used, should be lifted and sutured with their long axes always parallel to the lines of the normal muscle pull of the underlying muscles. If this is disregarded, secondary scars may develop, which are quite unnecessary. If massive defects need cervical flaps Snydecker's principle of delayed transfer of flaps is used. Massive deformities, involving both the conjunctival as well as the skin surface of the lid, must be corrected with mucous membrane upon the posterior surface if the eyeball is still intact and worth saving. One may not, under any circumstances, permit epithelium to come into actual surface contact with the cornea, nor to lie juxtalimbic. If the eyeball has been lost and enucleated, then both the anterior and the posterior surfaces of the reconstructed lids may be covered with epithelium. Figure 43 shows a patient with such a condition. Figure 44 shows the correcting pedicle flap after it had been lined by an epithelial pocket, lifted, and resutured into position to enhance its nutrient supply. Figure 45 shows the flap lifted and attached to the remains of the lower lid; in Figure 46 it is attached to the remains of the upper lid; in Figure 47 after resection of the pedicle and a horizontal incision for the palpebral fissure, the patient is wearing an ocular prosthesis. This reconstruction of orbit and lids can be done by first lining the orbit with a graft as for a contracted socket, thereafter by using the pedicle flap for the external surface of the lid. Pedicle flaps with either a mucous membrane or a skin posterior surface are formed by first making a pocket lined with epithelium or with mucous membrane at the position from which the correcting head of the flap is to be lifted. It may be wise, in all these

cases, to lift the flap and then to resuture it in its original position once or twice, wholly or in part, before it is finally transferred to its correcting position. This enhances tremendously its nutritive blood supply, hence, its viability.

When conjunctival defects accompany a lid defect and the flap is not the correcting procedure to be used, a free mucous membrane graft for the conjunctival defect should be the first procedure. Symblepharon with partial lid damage as an accompanying ectropion is the usual example of such a situation. Intermarginal adhesions are a necessary step in the free skin correction of ectropion, and these should not be released until all scar tissue contraction has ceased.

Defects for correction in which there is no deficiency of soft tissue must depend for success upon a complete removal of all cicatrix. The necessary undermining cannot be done unless it is adequate. This is seen in such instances as cicatricial ptosis and contraction lagophthalmos. When a free skin graft is to be used, adequate scar resection is an important factor. The inability to achieve this is perhaps the outstanding indication for the use of a pedicle flap. During the dissection for releasing a cicatricial defect, one must release with great care such structures as the orbicularis fibers, the canthal ligaments, the lid margins, and especially the deeper muscles responsible for the normal lid folds—the levator palpebrae in the upper lids and the lower crescentic fibers of the orbicularis. Following the normal lines of tissue cleavage simplifies a dissection decidedly. Pedicle flaps are indicated in situations where it is impossible to release or remove all scar; hence, this matter of scar resection is least applicable to that procedure.

The repair of a contracted socket, the result of a traumatic enucleation, always is accompanied by dense scars and the loss of considerable conjunctiva.

In these, one must remove boldly all cicatrices in the orbit. The dissection should form an inferior cul-de-sac level with the lower rim of the bony orbit—incising the periosteum there (not to have an inferior cul-de-sac of this size later, but to form a sheet of scar tissue adherent to the periosteum which will assist in maintaining a satisfactory inferior conjunctival fornix). The dissection into the superior fornix must pass up and backward, but sparing the levator palpebrae; otherwise, ptosis will result. Figure 48, a, b, c, d, illustrates two such situations. In a and b the lower cul-de-sac alone was lost; in c and d, the entire socket was replaced by a dense obliteration of scar.

When the graft is cut, to cover the mold and to fit as to the size of the dissected socket the surgeon must be certain that the entire surface of this mold is covered. Excess graft adjusts itself by necrosis and lysis, but an inadequate graft simply means fresh scars and adhesions, granulations, and an unsuccessful result from the surgery.

Cicatricial enophthalmos as the result of a retrobulbar posttraumatic suppurative cellulitis is a not uncommon and most distressing situation. Little if any surgery can be done to restore the lost ocular motility. The fixation which is present is a combination of true ocular motor nerve paralysis, actual destruction of the ocular muscles, and muscle—Tenon's capsule—eyeball cicatrices. If usable vision is still present, it is worth while attempting to correct the enophthalmos. The position of the eyeball can be improved by transconjunctival internal and external canthal angle incisions, the resection of the scar, certainly its wide release, and the introduction of rolled bolsters of tensor fascia femoris retrobulbarly. Some of these can be placed between the muscles and the eyeball, and others, especially above and below, between the muscle and the roof and/or the floor of the orbit.

The postoperative dressings for plastic cases are important. Free skin grafts must be applied with a fair amount of pressure with a dressing which will not creep. A splint of dental stent molded to the defect just before the graft is placed seems to be most satisfactory. The pressure dressing of a pedicle flap should not be as firm as for a free skin graft, and it must not compress the nutrient pedicle. Free mucous membrane grafts into the conjunctiva can be held in accurate approximation for several days after operation by means of a silver conformer, perforated in the center, so that the conformer is not in contact with the cornea. Absolute hemostasis is necessary before any graft can be placed in position or any dressing applied.

In the late treatment of these soft tissue defects, one must not lose sight of the important rôle which adequate massage can play in minimizing scars and releasing those already present.

HISTORY AND PRESENT STATUS OF OPERATIONS ON THE LABYRINTHINE CAPSULE FOR OTOSCLEROSIS

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THE results in hearing obtained by fenestration of the horizontal semicircular canal present problems which are still mostly unsolved. This surgery has opened new vistas of inquiry and research. It has demonstrated the paucity of our knowledge of the physiology of hearing. It brings into serious question concepts on diagnosis and classification of hearing defects hitherto held as established.

We are wont to consider surgery in the light of the relief or cure it affords for pathological lesions. In the type of surgery I am discussing, the restoration of a physiological function toward normalcy is the goal sought. The concept that by a surgical procedure the microphonetics of the structures of the ear shall become re-established to function normally and cause a deafened patient to hear presupposes a comprehension of these. In this premise lies most of the handicaps in this field, under which the otological surgeon works.

Surveying the exploratory surgical efforts to achieve successfully restored hearing acuity, I find that obstruction and confusion have been brought about by the record of many observations and postulates which, from a scientific standpoint, are unacceptable.

There is difficulty in summarizing end-results from this operation. The operations are recorded. The obvious successes and failures can be tabulated. The operations done by one man can be added to those done by another, and a grand total of successes and obvious failures can be summarized, but still that leaves us no nearer a solution of the problem, because there has been no standard criterion for the selection of cases for operation. Different types of cases are included among the successes as well as among the failures after surgery.

In other words, it is almost impossible to establish a standard for the "comparison of similars." Inherently the cases differ, although the deafness is seemingly similar. The same audiometric findings are possible in deafness of varying causation. It must be assumed that each surgeon has set for himself a criterion to indicate that operation would be successful. Then why in the same hands, and with the same technique, do failures occur? I have done exactly the same thing on successive patients and in each instance have employed the same criteria in selecting the case for operation, yet failure resulted in some while in others there were astonishing successes. I assume that the difficulty has its origin in the fact that this surgical procedure is aimed at restoration of function and not at removal of the pathological process.

Notwithstanding these considerations, the literature reveals attempts to sum up the totals of results from different surgeons. Of course, deductions thus made are open to scientific skepticism. In fact, this scientific skepticism has a place in evaluating case reports from any individual source which reports too large a sum total of material, all classified as otosclerosis and reported as having been operated on, successfully or unsuccessfully, as the case may be. In such reports, I see an endeavor evident to make a diagnosis based on pathological condition in the deafened patient, and to mark up success or failure on his functional activity. The lessons which the surgical procedure might teach regarding functional rehabilitation are minimized or lost. It is an assumption that the technical steps of this procedure are based on proved concepts. It is likewise assumed therefore that if the surgical steps in the technical procedures are properly carried out, the expected favorable end-results on functional restoration will be accomplished. The reason for this paper is to help clear up the misconception as to the present status of surgery for otosclerosis.

The exact clinical diagnosis of otosclerosis is almost impossible; in fact in most of our otological institutions the number of cases definitely diagnosed as otosclerosis is small. I myself still use the Lucae triad of raised lower tone limit, prolonged bone conduction, and a distinct hereditary factor as criteria for the classification of cases. Among those patients with chronic progressive deafness I find many who cannot be said to be deaf because of otosclerosis, according to the Lucae triad. Hence it is safe to assume that even

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in a given surgeon's practice patients of inherently different categories have been subjected to a specific operation, and the successes and failures recorded as the result of the procedure rather than as a result which would naturally follow in a specific type of case. Holmgren may be excepted from this criticism.

Too much stress, particularly in America, seems to be laid on a definite technical procedure and its minutiae. There is further confusion because fundamental factors concerning the surgery of otosclerosis are being complicated by an effort to popularize an endaural approach to the goal of operative endeavor—the fenestration of the horizontal semicircular canal and the covering of such fenestration by a tissue the external surface of which shall be in contact with sound waves and which shall aid in re-establishing better microphonetics in the deafened ear.

Whenever bone tissue or soft tissue is traumatized, whether accidently or surgically, healing ensues. After surgical fenestration and covering, the goal sought is the achievement of healing without regeneration of bone which would close the fenestration.

Success or failure needs consideration from various aspects. First as to healing, the wound made must heal promptly, with a dry ear, an intact drum, and an epidermized wound cavity. Second, as to function, success or failure cannot be judged wholly by the ability of the fenestration to remain patent; patency is estimated by producing a positive reaction to the fistula test when the site of the fenestration is touched with a cotton-tipped applicator. At re-operation, I have observed definitely open bone fenestration although the findings on fistula tests were negative by touch. In one such patient, even touching the exposed membranous labyrinth with a cotton-tipped applicator failed to elicit either nystagmus or vertigo. This patient, when subjected to the Barany labyrinthine tests, showed normal function of all semicircular canals. Let me emphasize here that the lack of a positive fistula response on touching the site of fenestration should not always be assumed to imply that the fenestration has closed. In many cases it has closed, but in others the surgical procedure was successful. Other factors have produced the negative reaction to the fistula test, among which may be mentioned local labyrinthine adhesions walling off the site of the fenestration from the rest of the membranous labyrinth.

Furthermore, the postoperative positive reaction to the fistula test when the site of the fenestration is touched is not a sure indication that the functional re-establishment of hearing acuity has been attained. In patients operated upon by others as well as in some of my own, although at repeated examinations I have invariably obtained positive fistula test reactions, the hearing acuity has remained unimproved since operation. Therefore when a positive reaction to the fistula test is used as the sole criterion in estimating the case as a success the observation is unsound. The surgical technique may have been successful in keeping the fenestration open, but the result as to restoration of hearing should nevertheless be considered a failure. From these observations the conclusion is inevitable that the maintenance of a patent bony fistula *is not the sole factor* necessary to improve hearing acuity, or, conversely, that all patients do not show functional hearing improvement when a fenestration is made and maintained in the horizontal semicircular canal.

The dramatic demonstration of suddenly acquired increased hearing acuity at the operating table at the moment when the perilymphatic space is entered has little scientific implication, and no deduction should be drawn from it. It is more important that the surgeon visually recognize the penetration into the perilymphatic space than place reliance either on the suddenly exhibited nystagmus or on the increased hearing acuity because, if the membranous labyrinth has been accidently injured, the dramatic exhibition would nevertheless be present. The absence of all these phenomena because of deep general anesthesia or somnolence from hypodermic medication during local anesthesia, however, does not preclude good after-effects and a satisfactory end-result, as some of my cases demonstrate.

HISTORICAL DATA

It manifestly is impossible within the reasonable scope of this paper critically to annotate and document all pertinent publications which in their successive appearances in otological literature since 1779 trace an *evolutionary progression of development* of this type of surgery for the improvement of hearing acuity. I will content myself with a brief account of the principal contributions up to the one stage endaural technique. Recent reports will be touched upon only as they present factual observations bearing on the present status of this type of surgery.

Since 1779 propositions, techniques, and case reports have appeared revealing attempts to improve hearing. These range from efforts to achieve permanent openings in the membrana tympani, to tenotomies of both the tensor tympani and the stapedius muscle, to extraction of

the malleus and the incus and even efforts to extract the stapes.

In 1877 Kessel (18, 19) removed the stapes, and thus opened the osseous labyrinthine channels. A transient improvement in hearing resulted. In 1897 Passow reported that he had constructed a protective drill with which a hole could be made in the bone of the promontory, just below the oval window and adjacent to the insertion of the foot-plate of the stapes. The immediate results on the hearing acuity were amazing. The tinnitus also disappeared. These improvements were found to be transient, however, and because of the opposition of Pollitzer, Cazzolius, Lieberman, Botey and Denker—all great authorities in otology—the operation was discarded.

In 1898 Alderton opened the labyrinth at the oval window. Only temporary hearing improvement resulted. Faraci in 1899 reported having operated upon 11 cases, after extensive animal experimentation. He made fenestrations in the cochlea by removing small sections of the rim of the oval window. His reports were, on the whole, favorable. In the same year, without knowledge of the work of Passow, after opening the promontory, he placed a Thiersch graft over the fenestra. At first the hearing was good, then equivocal. In 1899 Floderus also, without knowledge of Passow's contribution, after extensive cadaver studies, employed for the location of the fenestra, the ampulla of the external horizontal semicircular canal, near the bony lamella bounding the vestibular perilymphatic cistern of Retzius. What his functional results were are not quite clear from his report. In 1913 Jenkins (14, 15, 16) reported on 2 cases upon which he made fenestrations in the horizontal semicircular canal. For a covering he used a Thiersch graft in one case, and in the other employed a skin flap made from the external auditory canal wall. His improvements in hearing acuity were transient, and the end-results were somewhat better than before operation. In 1914 Barany suggested fistulization of the posterior vertical semicircular canal. He showed that improvement of hearing was procurable, but the results lasted only a few days. In 1917 Holmgren, after making a fistula, immediately covered it with an elastic membrane. The fistula was placed at the upper part of the anterior vertical semicircular canal, after the bone between the dura and the fistula was removed and the dura was allowed to act as a covering for the fenestra. The hearing in one patient, thus operated on, was good. The result, however, was only transient. Holmgren suggested another feature; the excision of a piece of the dura and the use of the arachnoid membrane as covering material. This was, as far as I am able to ascertain, never performed in a living patient. In 1917 Holmgren operated on the promontory of the cochlea and used a mucoperiosteal flap for covering tissue. Reporting in Paris in 1920 Holmgren conceded that his results as to improved hearing were only transient, and his end-results were negative. In 1923 he reported that while the improvement in hearing was not permanent, it lasted a longer time. During the course of observation of patients operated upon, he noted a progression in the hearing loss in the ear not operated upon, but that in the ear operated upon the hearing did not go below the level held at the time of operation. In other words, the progressive loss of hearing seemed stopped in the ear operated upon, even though hearing in this ear did not permanently improve.

About 1922 Fremel reported a case in which he had made a fenestration in the posterior semicircular canal. The improvement in hearing was transient, but the hearing loss remained stationary on the side operated upon.

In 1924, Barany made the first report of a two-stage operation. The first stage was an antrotomy and fat was placed in the cavity. The wound was permitted to close and heal. After 4 to 6 weeks, the cavity was re-opened, the horizontal semicircular canal exposed and opened. The previously placed fat tissue was pushed into the fenestra, and the wound reclosed and healing allowed to proceed. But Barany, working with gouges and without magnifying glasses, could hardly avoid little traumas to the membranous labyrinth and small hemorrhages into the lumen in the canal. In Barany's technique, it is to be noted that after opening the canal, he first implanted a piece of fat and thus blocked the opening, then he enclosed the fat and the opening with a piece of rubber dam about the size of a pea; to make it kneadable he warmed this piece of rubber dam and pressed it into the opening of the fistula. The results as to hearing were primarily good. They lasted only 2 weeks, however. He reports his results as follows: Directly after the canal is opened, the hearing increases from near the concha, where voice is heard before operation, to a distance of several meters. After the canal opening is closed, an appreciable loss of the newly acquired hearing is noted. Nevertheless hearing is still better than before operation, for conversation is comprehended at a distance of several meters.

About 1926 we again find Holmgren attempting a fistulization of the horizontal semicircular canal, which he immediately covers with the

mucoperiosteum of the ampulla. This resulted in a very great improvement in hearing, which lasted for a few weeks. In some cases improvement in hearing was not so marked, but it lasted somewhat longer.

In 1924 Sourdille (27) reported on fenestration of a horizontal semicircular canal. His is a multiple operation. In the first stage he explored the middle ear and attempted to isolate it. He termed this procedure an atticotympanotomy, simple or combined, with an internal plastic with a tympanic hinge. At the second operation he opened the external horizontal semicircular canal and occluded the fenestration by a thin epidermic membrane. Each stage of the procedure was done under local anesthesia and with strong adrenalization. Because of what followed it seems wise to give the details of the pioneer work of Sourdille. He not only merits the distinction of having persisted in the search for a solution of this problem, but he is credited by Holmgren with having restimulated him after "failures" again to study this problem. Sourdille's technique embraces the following: (1) mastoid trepanation, with careful elevation of the soft parts of the external auditory canal from the bony canal wall; (2) mobilization of the tympanic membrane only in the upper half of its circumference, with the cutaneous lining of the external auditory canal; (3) a resection of the "osseous bridge" of the external wall of the attic, and of the tympanic ring, corresponding to the portions of the tympanic membrane which he mobilized. This done, a larger view of the attic, the tympanic cavity, and the ossicles is obtained. This procedure he terms "simple atticotympanotomy." It permits exploration of the fenestra ovalis and the lesions of the ossicle. (4) Removal of the body of the incus with or without resection of the head of the malleus. This step he terms "combined atticotympanotomy." (5) His "internal plastic." With a tympanic hinge the flap obtained from the posterior superior wall of the membranous canal is lowered inward and placed against the internal wall of the attic. By its adherence to the attic wall the tympanic cavity is hermetically closed and separated from the mastoid region. There then ensues an interval during which epidermization takes place in the opened parts of the mastoid cavity.

A few months later the second stage is undertaken when the cicatricial lining of the mastoid cavity is sufficiently thin and transparent. Then trepanation of the prominence of the external semicircular canal is performed. This takes place in the following sequence of steps. (1) The retroauricular wall is reopened. A piece which is destined to be replaced over the opened canal wall, is traced and cut out of the cicatricial flap. The tympanic cavity is not to be reopened. (2) The prominence of the external semicircular canal is trepaned by rubbing with special rubbers made for this purpose. (3) The epidermic flap is placed over the new orifice of the fenestration, thus closing it and preventing any infection of the internal ear.

The first stage of Sourdille's procedure is not concerned in improving hearing, but is merely a preparatory measure to provide a means of closing the labyrinthine fenestration. Sourdille, however, does report that he has observed a slight amelioration in deafness, *more marked in the opposite ear* (italics mine). He also observed diminution of the previously present tinnitus in both ears. During the second stage of the multiple surgical procedure, he makes the following observations.

"During the operation no matter how thin the osseous wall of the semicircular canal may be, no improvement whatever of hearing takes place before the perforation of this wall. At the very moment when the operator perforates this wall, the patient complains of dizziness of short duration (from 1 to 2 seconds) after which he hears with incomparable clearness and intensity. This reappearance of hearing as well as the dizziness coincides with loss of a very small quantity of perilymph. This can only be seen under the microscope with a magnifying power of ten diameters. The improvement in hearing depends on many factors. . . ."

During one operation, Sourdille observed that hearing at the initial opening into the semicircular canal, which was very small, immediately was improved and the patient comprehended the low spoken voice at a distance of 40 centimeters from the ear. When the semicircular canal opening was enlarged hearing acuity was increased to 2 meters for the same spoken voice. In all his cases the low pitched sound was heard best. This was particularly true in patients in whom before the opening was made the high pitched tones were better heard. Sourdille makes the following additional observations.

"In order to make possible the perception of low speaking voice at a distance of 2 meters, at operation, it is necessary that the labyrinthine trepanation be laid open. If one covers it with an epidermic flap, immediately the voice is not perceived at 1 meter, or at 80 centimeters, or even at less distance. The maximum audition seems to correspond to the penetration of the sound waves through the labyrinthine fistula thus made. If, now, I apply paraffin gauze, covering alternately the tympanum or the epidermic flap, I obtain, according to the former degree of deafness, and the state of the flap, hearing equally well by the tympanum or by the labyrinthine trepanation. This indicates that hearing can be perceived equally by the tympanic route

and the fenestra rotunda, or by the labyrinthine orifice and the scala tympani.

"If I cover the tympanum and the orifice of the labyrinthine trepanation at the same time, the low voice can even then be heard at a few centimeters and the high pitched voice is understood with an intensity and a clearness unquestionably better than before operation. The Schwabach has the same value as before, and the Rinne remains negative."

Sourdille believes that the end-results depend entirely upon the condition of the flap; if it remains thin, closely applied, the improvement of hearing lasts without change.

Immediately following Sourdille's presentation before the Royal Society of Medicine, Mr. Harold Kisch (20) reported that he had performed some operations in cases of deafness and catarrhs of the middle ear. He had considered the question whether or not to make the new opening through the semicircular canal or through the promontory. He had decided on the latter. He employed a simple method, exposing the middle ear and then using a small trephine worked from a dental engine. He entered the promontory, the outer wall of which he removed. He immediately closed the gap of the promontory, using a skin graft taken from the thigh. At a session of the Royal Society of Medicine in 1912 Kisch demonstrated 11 cases. His end-results could not be reported as during the first World War his papers had become lost and the patients scattered.

In 1936 Holmgren (11) reporting to the Third International Oto-Rhino-Laryngological Congress in Berlin, made a report on surgery for otosclerosis. His procedures then were as follows:

Under local anesthesia a wide antrotomy is performed with most careful hemostasis. The anterior lateral wall of the saccus endolymphaticus is then uncovered. At this point in the operation, he notes an immediate improvement in hearing. Then, preferably using a chisel, fistulas are made in the horizontal and in the posterior vertical semicircular canals. Sometimes he also puts an opening into the anterior vertical semicircular canal. Each fistula is made fairly long, 4 to 5 millimeters. The endosteum is removed without injurying the membranous labyrinth, and the fistula is widened as much as possible. As soon as the fistula reaches a canal, the hearing increases promptly and constantly; in fact, all patients hear afterward conversation at greater distances than the length of his operating room. They hear at least at distances of 10 meters. He now enlarges the aditus ad antrum and a soft prosthesis is laid into the antrum and into the fenestrations, which Holmgren believes prevents collection of blood and wound secretion, and supplies an elastic wall for the fistula. This prosthesis is so placed that it crowds the openings made somewhat, to prevent closure during the healing process. As prosthesis he employs various substances—a thin rubber bladder (filled with air, a physiologic salt solution, or fat), a piece of gutta percha, or more recently fat tissues. In addition he also reports that he has coated the antrum with gold leaf and then put the fat prosthesis on top of this gold leaf. He believes that this prevents an undesirable growth of the fat tissue to the membranous labyrinth. Everything being placed in position, he closes his original incision with Michel clips and secures healing by primary union.

Holmgren makes the following observations:

The improvement in hearing at the time of operation is constant and astonishing. During the period of healing hearing is reduced in some cases to the pre-operative state; twice he found it even worse than before operation. In the majority of his cases [he reports on 34 in this communication] a greater or lesser improvement in hearing is attained, which in certain cases is even progressive.

In October, 1937, Sourdille (28) came before the section of otolaryngology of the New York Academy of Medicine and reported on his latest procedures and summarized his cases. Sourdille now proposes a surgical technique which usually consists of three stages but sometimes requires more than three stages.

The *first stage* is performed entirely within the external canal. It consists in lifting the cut thick cutaneous soft parts, fibrous bands, and periosteum of the posterior superior semicircumference of two-thirds of the external auditory canals. The operation to accomplish this, however, is carried out through a postauricular incision. It may be done through the external auditory meatus, provided this is sufficiently wide. The interval after this procedure is utilized to obtain surface of membrane from which periosteum has been removed, a supple cicatrix, but resistant and without sebaceous glands. The time which generally elapses to accomplish this he puts at between 6 to 8 weeks. The *second stage* is carried out entirely in the middle ear. An incision is made through the original postauricular scar. The previously made thin cicatrix is separated from the posterior superior canal wall. The cicatrix is now found to consist of new skin and scar tissue and also of the upper border of the drum. This step Sourdille calls an "internal plastic." Next a resection of the mastoid process is undertaken and the aditus and attic completely exenterated of all cell structure, thus bringing into view the incus and the head of the malleus. The joint between these two parts is opened and the ossicles separated. Then the head of the malleus is carefully resected, caution being observed not to injure or puncture or tear the membrana tympani or to displace the incus which should be maintained in its high lying position and its posterior and its inferior articulations conserved. The previously prepared flap is then elevated and its bleeding surface applied to the incus, its internal surface to the attic and the aditus, and as far as it will reach placed over the floor of the antrum. The middle ear is thus hermetically

sealed in its superior portion. The procedure is ended by covering the lower part of the exenterated mastoid cavity with an external plastic flap made up of scraps of skin and muscle elevated from the inferior surface of the mastoid process.

Now a second interval of time is allowed to elapse of about 6 to 8 weeks, and observations are made of the transformed ear through the external auditory canal. Generally the meatus will be found widened and communicating directly with the mastoid cavity. A large vestibule has been formed behind the curve of the horizontal semicircular canal which is covered by a more or less thin cicatricial pedicle of cutaneous tissue. This is found communicating with the modified tympanic system now found comprising the membrana tympani and the so-called "internal plastic," the surfaces of which are continuous in their superior half circumference.

The *third of labyrinthine stage* consists in lifting up the endomastoidal flap at the level of the external semicircular canal. This canal is then opened, extreme care being exercised not to injure the membranous labyrinth. As soon as this opening is obtained, there is noted an increase in hearing 10 to 20 times better than the pre-operative hearing acuity. The cicatricial endomastoidal flap is now replaced over the fenestration. Sourdille makes the following observations regarding the hearing.

The hearing which ordinarily has been decreased in the days immediately following the operation, when cicatrization is complete, is measurably increased. It is better even than that observed on the operating table. With tuning forks, the return of aerial hearing for low pitched sound (64 and even 32 double vibration forks) are heard. The Weber is changed, lateralization toward the side not operated upon and even the Rinne can be positive on the side operated upon.

Sourdille remarks that "unfortunately the success is ephemeral." In from 4 to 6 weeks he has observed that the aerial hearing diminishes, the Rinne test reaction becomes negative and the results of the Weber test equivocal. He thinks this is due to closure of the labyrinthine fistula, because of the reconstruction of rigid bony deposits which close the fistula.

These bony replacements, Sourdille considers, do not attain the thickness of the primitive bony canal wall. In most instances they do not attain thickness of more than a few tenths of a millimeter. Therefore, he undertakes a supplementary operative procedure to remove this bony film. This he calls "touching up an operation." The hearing is then re-established and often only then will this gain in hearing be lasting.

Sourdille's tabulation of results comprises 140 patients upon whom he operated about 400 times. The hearing results were very good (hearing improvement was measured by distance in which given sounds could be heard) and showed improvement in increase of distance of 10 times that of the status before operation. These equalled 40 per cent. Those whose hearing distance improved only 5 times that of the status before operation equalled 14 per cent. Recently through improved technique, he obtains good results in 80 per cent of his patients, and of these, 60 per cent show an increase in hearing distance 10 times that of what they had before operation. He had no fatalities in any of his 140 cases.

Following Sourdille's report Lempert described a new one-stage procedure which embodied all the features of Sourdilles' operation. He used burrs and claimed to use the Shrapnell membrane as covering for a fistula produced in the horizontal semicircular canal. His operations were performed endaurally. This was the first American contribution.

Other current reports are based on the pioneer work here reported. Otologists in this country and England are at present trying out the Holmgren, Sourdille, and Lempert techniques, but their cases are too recent to be of value in estimating end-results.

THE FUNDAMENTAL OBSERVATION

There is now available a very creditable record of surgery to improve hearing. In each and every procedure which is reported, it is recorded, and my personal experience substantiates it also, that as soon as the osseous labyrinthine capsule is opened, there is positive demonstration that the deafened patient hears better than before fenestration was undertaken. And this is observed in varying types of cases which exhibit deafness as a symptom, whether or not that deafness is caused by the lesion known as otosclerosis. This is an important scientific fact. Nor does this fact lose its significance if subsequently this initially improved hearing acuity is lost. This repeatedly observed fact upsets our ideas regarding the pathological lesions which, from audiometric tests followed by histopathological studies have given us a conception of the lesion held responsible for the deafness. In other words, if the lesions rendered the patient deaf, how account for the immediate recovery of the function of hearing upon fenestration in an exactly similar case? Surely it may be surmised, if these studies are

correct, that similar lesions are present in the hypothetical case cited, and we know that the effect of a fenestration operation does not immediately reach ganglion cells in the cochlea. This premise may be stated, thus: patients complaining of deafness and tested by the means at our command—the audiometer, forks, voice, etc.—are actually deaf only in relation to the media used to test them. Even those greatly deafened, who by the means we employ to test them show what are called islands of total deafness, are not actually deaf for this sound wave frequency, because often when the amplitude of vibration of the same sound wave frequency is greatly increased—as for example by use of an organ-pipe—these patients will hear some note. Probably an actual acoustic nerve lesion with its accompanying dysfunction is the only exception to this generalization. In this connection it is of interest to note that Lucae believed that even when he had positive evidence of stapes ankylosis this finding did not indicate that the patient was actually deaf. So profound a student of otosclerosis as Albert Gray, of Glasgow, wrote in 1928 that the deafness of otosclerosis throughout a large part of its course is due "rather to suspension of the function of hearing than to its actual destruction."

The retention of the newly gained improvement in *hearing acuity* constitutes the very essence of the problem which this method of treatment seeks to solve. *One way to achieve this* is to devise a means *to maintain the surgically made fenestra in the labyrinthine wall.* Let me at once add that *not in all cases* in which this surgically made fenestra remains open, does hearing acuity remain at its initially acquired improvement level, but in some instances it gradually drops to its prior level of recorded hearing loss. As a corollary, therefore, the *second fundamental* problem for solution is to find the means to differentiate between the cases prior to surgical intervention. The finding of a permanently maintained open fenestra giving a positive fistula reaction, a healed surgical wound, an intact tympanic membrane and open eustachian tube, totally *unaccompanied* by maintenance of improved hearing acuity, leaves the situation unsatisfactory. The success or failure of enduring results of the procedure still remain *unpredictable*, and the patient even in the most competent hands, must take "the gamble" on the expected results.

EFFORTS AT MAINTENANCE OF AN OPEN FISTULA

Because of the obvious finding that, when fenestration is done and the surgically made window remains open for a time, hearing acuity also is improved, it is easily comprehended why such intense efforts have been made to keep the fenestra open.

The studies may be divided into groups. The surgical studies of Holmgren (13) are noteworthy. A fistula covered with subcutaneous fat in 1 patient resulted in improved hearing for 2 years. Holmgren also tried covering the fistula with a mucoperiosteal flap and with gold leaf; and a tissue lined with connective tissue and covered with pavement epithelium was also employed. He has not yet reported the results obtained from the last set of experiments. Regarding technique he recommends that the periosteal layer of the labyrinthine wall be removed as far as possible. The endochondral layer will not heal and the endosteal layer and endostium should be removed as completely as possible. The semicircular canal should be opened on its concavity or at its side. He experiments with the application of prolonged pressure to produce pressure erosion; he suggests plugging the haversian canals in the bone with bone-dust, and also suggests the use of electrolysis through the application of various metals to prevent bone regeneration and encourage bone atrophy. Finally, he is now experimenting with irradiation through the application of radium or mesothorium. To date, nothing of positively definite value is available. The experiments are not concluded, and for Holmgren the question still remains unanswered.

Sourdille (28) has a very complex technique to maintain patency of the fenestra. In substance it consists in the use of a connective tissue flap covered with pavement epithelium. After repeated revisions which he euphemistically terms "touching up" the site of the fenestration by removing newly formed bone lamellae which close the area, he eventually has some remain open because he says he "exhausts the regenerative power" of the bone. I record what he states but doubt the scientific value of the reasoning. Lempert (23, 24) established a postulate in his reports in which he stresses that covering the fenestra with Shrapnell's membrane *is the necessary factor for success* in keeping the fenestra open. Additionally, the use of polishing burrs and burnishing burrs and of a 24 karat gold burr to impress gold dust particles into the exposed bony surfaces is advocated. Most anatomists and many otological surgeons have serious doubts as to the possibility of stretching Shrapnell's membrane to reach and cover the fenestra placed in the horizontal canal. Lempert's own failures and reported revisions in themselves lessen the strength of his contention, to say nothing what-

soever of Sourdille's report of 74 per cent successes in 140 patients. Sourdille never employed any kind of burr in any of his cases, and he makes no pretense of employing Shrapnell's membrane to cover the fenestration. His record, on its face value, is every bit as impressive as Lempert's. Incidently, Lempert's first report of having operated on 23 patients of whom 22 had persisting fistulas needs revision when his Boston presentation is studied. In this report the failure to maintain an adequate fistula among these 23 patients amounts to 39 per cent. It is presumed that he employed not only the burrs but also the so called Shrapnell membrane as coverage. Holmgren also suggested employing the dura and the arachnoid over the superior semicircular canal, which he had fenestrated. Employing the dura in some instances and the arachnoid in others, he used a tissue which contained no periosteal stroma; nevertheless the fistulas closed, and the hearing acuity reverted to that before operation. One is forced to the conclusion that the regenerative power of the bone itself is the factor at fault. This factor, which is nature's method of repair, must needs be nullified or guided in some way if success is to be achieved in keeping the fenestra open.

As a matter of fact, there are successful cases on record in which fenestration was done by different instruments and by the use of different tissues to cover the fistulas. Among those who used other tissue than Shrapnell's membrane is Campbell. The Guggenheims report a case which they observed, and they state specifically "that the claim that the pars flaccida, or Shrapnell's membrane, is used to cover the fistula is not accurate." Among my own cases, I have never been able to get Shrapnell's membrane to reach far enough to cover the newly created fenestra in either those which I term successes or those which are not. I do not think that Lempert's contention in regard to this factor in his technique will stand the test of time and experience.

The experimental studies of Canfield and the Guggenheims, while valuable contributions in themselves, leave the main question still unanswered. Canfield endeavors to solve the question as to what differences occur in the surgically traumatized bone by the experimental effects of the instruments used in the surgery. The influence of heat and friction from the burrs, the injury to bone cells by the burr, and the possible diminution of the bone's regenerative power—these all engaged his study. He concluded that the response of vital periosteal bone differs significantly when defects are made with different instruments, even when the defects were universally covered with the same tissue. According to Canfield, the essential point in keeping the fistula open is the management of the bone itself with less regard for the nature of the tissue placed over the defect. Canfield credits the burnishing burrs with inhibitory power over bone regeneration. The Guggenheims, on the other hand, fail to substantiate this contention.

Neither the Canfield nor the Guggenheim experiments were carried out upon semicircular canals. This raises objection to conclusions drawn from these experiments. The Guggenheim report, however, anticipates this criticism by stating: "The fact that the labyrinthine capsule consists of both membrane and cartilage bone in no way affects the experiment, as all new bone formation, whether in the labyrinthine capsule or elsewhere, is by membrane-bone process. The ontogenetic phenomenon of the transformation of cartilage model into bone model is *strictly* an ontogenic occurrence, and never a repair process. . . . In the final analysis of osteogenesis in artificial fistulas, the individual characteristics of primary germinal tissue (mesenchyme) will doubtless prove to be the determining factor just as they are in such conditions as chondrodystrophy and osteogenesis imperfecta and in connection with individual potentialities for fracture healing." Believing osteogenesis can be impeded by vitamins, Kend has undertaken a study of diet with combinations of vitamins to inhibit bone regeneration. Although his reports are as yet unavailable he generously furnished me with his data, so that I might try them also.

To summarize it can be said that no way to keep the fenestra open has yet been devised which successively applied will successively give similar results. Neither the use of burrs nor the application of a particular tissue to cover the fenestra assures positive results in succeeding cases with any degree of certainty. This is true whether in reference to the cases of one surgeon, or of different surgeons. Conversely, good results are reported by different surgeons who have used different instruments to make the fistula and who have used various types of tissue to cover the fenestra.

I am still as much at a loss to account for the successes I have had as I am unable satisfactorily to explain my failures, for I have used similar technical procedures in either instance and have encountered no untoward happening to complicate the issue. In other words, I cannot predict the probable outcome in a given case because as yet there are no criteria available upon which to

predicate success, nor have I found anything in the published reports of other workers, which would make prediction of end-results more certain. In passing, I may remark, that I have encountered untoward happenings in some of my cases—torn flaps, perforations of the membrane tympani, and secondary infections of the middle ear spaces—all of which, if the current literature is to be credited, should have doomed the patient to ultimate deafness; yet in some of these patients there was a persisting open fistula with improvement in hearing acuity. Why? I cannot yet find the answer.

THE RÔLE OF THE INCUS AND THE EPITYMPANIC SPACE

The rôle of the incus is still unsettled. An ankylosed stapes articulated with an incus but disarticulated from its connection with the head of the malleus when the head of the latter is amputated, as is done in the currently employed techniques as first suggested by Sourdille and now part of the so called Lempert operation, leaves the question of what use does the retention of such an incus possess. One of the best functional results I have thus far obtained from this operation was in a case in which the incus was removed.

I may add that studies on the rôle of the incus are in progress, and when deductions are warranted report will be made. The entire question as to the necessity of surgically disturbing the tympanic and epitympanic structures is under survey. Prompted by the work of Sourdille, a reconstruction of the tympanic cavity, a resection of the head of the malleus, and its necessary concomitant—opening into and partially obliterating the epitympanic space—are now the operation of choice. This popularity has resulted from the incorporation of part of Sourdille's work in the technique advocated by Lempert which not only he but all his pupils follow without actually comprehending why. The scientific reasoning upon which these procedures are based is totally unconvincing and the theories are not proved by factual observations. There are reports of temporary improved hearing acuity in cases in which neither the head of the malleus nor the epitympanic space was involved in the technique. Of course, failure eventually resulted in such cases as regards permanently improved hearing. These failures were due to closure of the fenestration and did not depend in any way upon the technical procedures upon the epitympanic space.

As has already been recorded in my preliminary report, in some of my patients fenestration has been done without surgically touching any of the epitympanic and the tympanic structures. In others I have followed Sourdille's suggestions and have amputated the head of the malleus and obliterated the epitympanic space. A sufficient number of patients has not been operated upon and the time elapsed since operation is too short to permit a comparison of results at this time.

Another observation regarding tympanic structures, the epitympanic space, and the ossicular chain should be mentioned. In a preliminary report a year ago, I presented audiograms taken before and after fenestration in a patient upon whom radical mastoidectomy had been performed in 1918. At the time the patient came under observation, the ear had been dry and healed for years. In an endeavor to better his hearing acuity, with the patient's consent, I performed a fenestration upon his ear. The ossicles, and the tympanic structures were missing as a result of the well performed radical mastoidectomy. The old wound area was covered with a thin epidermized lining and this was used to cover the fenestration. Healing rapidly ensued, and the ear was dry. The fenestration was open and gave a positive fistula test. Hearing acuity was very definitely improved as shown in the audiometric charts and in the conversational ranges. Figure 1 shows the maximum improvement obtained. Hearing improvement was maintained and the fistula remained open almost 8 months, then gradually the fenestration closed, and hearing acuity dropped to that before operation.

The improvement in hearing acuity, transient though it was and dependent upon keeping the fistula open, is a fact of great scientific significance. It is a fact that the early pioneers in this type of surgery obtained temporary improvement in hearing acuity upon performing fenestration. This fact has become the basis of all the elaborate techniques since laboriously built upon this one outstanding scientific observation. Therefore, we must study and evaluate the fact established by my observation, namely, that in a patient with the tympanic cavity missing, with the external wall of the epitympanic space ablated, and with the malleus and the incus absent, the fenestration of the horizontal semicircular canal resulted in improvement in hearing. The later loss in the newly acquired hearing acuity paralleled and coincided with the gradual closure of the surgically made fenestra. Do not these observations make us doubt the accuracy of our present concepts as to the rôle which the tympanic cavity and its ossicles play in the inherent acts concerned with hearing? We must build our knowledge from this observation as a basis. In my opinion the

maintenance of the fenestra is the greatest technical factor in retaining hearing acuity and all additional details upon which so much stress has been put, seem less important in the solution of our problems. I shall not here discuss the newer theory regarding the physiology of hearing which the observation just recorded and other studies under way suggest. In addition to this case I shall cite others each of which is a negation of the ideas which the most propagandized technique is tending to spread and because they demonstrate that comparable results are obtainable by totally different technical procedures.

Another observation is noteworthy. If one examines the bone conduction audiogram, taken under conditions of masking, in Figure 1 with 30 decibels of the same note as tendered to the examined ear, a loss in bone conduction is revealed, reaching its maximal loss at the 2048 frequency cycle. During the period in which hearing was improved and the fenestra remained open, this masked bone conduction was markedly improved, and this was true in more than one examination. If the accepted theory of how bone conduction comes about is to be maintained, then we lack a reasonable explanation for this finding. On the other hand, it is logical to assume that the improved bone conduction after fenestration is a factual observation and that our prior held concepts on bone conduction—how it eventuates and its significance when showing a loss, need review and study as to factors in establishing diagnosis. This observation brings into question the rôle played by the ossicular chain in presenting bone conduction. In addition the diagnostic criteria on the condition of the acoustic nerve which we are habitually wont to deduct from diminished bone conduction is also questioned. In my case, bone conduction was diminished but was improved after fenestration despite the absence of the major ossicles and membrana tympani.

THE METHOD OF SURGICAL APPROACH

I need add but a word regarding the endaural approach to the antrum and the epitympanic space. Inherently there are many reasons why I disapprove this approach. These reasons have no bearing upon the fundamental questions with which this paper is concerned. The postauricular route has many obvious advantages over the endaural route. I believe the sound judgment of operating otologists will bear me out in this premise. There is no step in this field of surgery that can not be more easily done with the postauricular than with the endaural route, whether it applies to the epitympanic space, the head of the malleus, the sulcus tympanicus to free the drum and make a tissue to use as coverage for the fenestra, and the fenestration itself.

DANGEROUS EXPERIMENTS

It may not be amiss to sound a note of warning regarding one experimental surgical effort, reported incidentally among a mass of other material. The merit of the procedure was never debated or even commented upon in the report of this work. I refer to the revisions undertaken by Lempert in the cases he lists as Cases 88, 71, 72, 97, 56, 8, and 106 in his Boston presentation. In these cases he employs pavement epithelium to cover the fenestra, turns the epithelial side toward the open bone wound, and attaches the blood supplied raw side to the meatal flap. He thus covers the fenestra with a membrane which does not attach itself to the fenestrated bone. This he contends retards bone regeneration. I am willing to concede that this may be true, but every student of medicine knows that pavement epithelium should never be buried in tissue but should be kept in contact with air, and it should be so placed that the inevitable exfoliation from pavement epithelium can find easy egress externally. To this fundamental conception of pathology I believe most plastic surgeons also subscribe. The reverse side of this implanted flap converts itself into living matrix, and Lempert actually is implanting the beginnings of future pseudocholesteatomatous growths if the graft lives. As we know, such growths develop slowly and these patients may eventually—unless our basic knowledge of pathology is at fault—come to grief because of the buried epithelium. What will happen then, as the result of pressure erosion from accumulated desquamation surgically located in contact with the membranous labyrinth, needs no prophet to foretell.

Another word of warning should be said concerning the Lempert reports. In his original publication, he reported 23 cases and of these only 1 fistula failed to remain open. In his second publication (Boston presentation), however I find that 9 of these same cases are listed as having required revisions, some more than once. Among these, in 4 vestibular function was lost or impaired. Among the additional cases included in the 120 patients upon which the second report is based, are 4 others which likewise suffered serous labyrinthitis. This serious outcome was the result of the operation itself and because of it, Lempert was prompted to state "revision of the fenestra involves a much greater risk to the

membranous labyrinth than does the original fenestration." With this conclusion I am fully in accord, and I have done no revisions after my first experience with one. In that case nothing untoward happened, but the dangers inherent in the procedure were so apparent that I have never attempted again operating upon failures, and I would warn the profession against permitting their patients to undergo such revisions. It is better that the hearing acuity revert to the status before operation than that the patient undertake so great a risk of losing his hearing and thus be unable to procure for himself the hearing improvement that an artificial hearing-aid apparatus could bring him. When this type of surgery was first proposed, Holmgren, Sourdille, and I minimized the risks of damage to the membranous labyrinth which are taken by patients under the precautionary aseptic surgical measures usually employed. All these surgeons prided themselves on an absence of any labyrinthine injuries and reported none having happened. This is particularly true of Sourdille who performed 400 operations, revising fenestrations often more than once. The meticulous care as to surgical minutiae and asepsis of which Lempert writes and speaks seems to leave us at a loss to account for the hazards to which his patients were subjected. No otologist of experience, I dare say, will minimize the danger which a serous labyrinthitis entails. Unless this type of surgery which carries with it the danger of labyrinthitis is controlled, we shall sooner or later be confronted with the tragedies subsequent to an established labyrinthine suppuration and meningeal infection. That this is a grave danger is evident when I point out that while Frederick estimated the usual occurrence of labyrinthine infection to be only about 1 in 100 cases of *middle ear suppuration*, in Lempert's report there were 8 labyrinthine infections in 120 cases.

SELECTION OF CASES

The literature furnishes few details which could be used to create a standard for the selection of cases which would be improved by this operation. Current publications imply that the deafness caused by otosclerosis may be helped. The diagnosis of otosclerosis is almost impossible to make clinically at the present state of our knowledge. Hence an approximation to such a diagnosis is all that can be hoped for. It becomes increasingly important, therefore, that prior to subjecting a given patient to this type of surgery a rather prolonged period of observation of the patient—if necessary, over a period of months—is desirable before the final decision is made. In such a study the impression gained by one consultation and examination is checked and rechecked; a clinical estimation of the patient is obtained; a comprehension of the mental and psychic make-up of the individual is developed; and ancillary examinations regarding endocrine disturbance, metabolic dysfunctions, and other pertinent factors become part of the case history. This period of observation often presents changes in the audiometric readings too; and ranges of variation prior to operation can be established. Usually every one working in this field agrees that good bone conduction, observed under conditions of masking, is at least a desirable condition; but that patients whose audiometric readings show a curve indicative of acoustic nerve dysfunction are not good prospects to submit to operation. Holmgren has suggested a detailed study of the drum and the external auditory canal in addition to the classical data to determine the presence of otosclerosis. This study should include: a consideration of the thickness of the skin and its dryness; an estimation of the amount of subcutaneous tissue; the presence or absence of cerumen; the rapidity of inducing, or the absence of, cough (tickling) and vascular reflexes; the movements observable of the membrana tympani—which segment moves most, what adhesion restricting motion can be demonstrated; and, finally, a minute study of the movements observable in the ossicular chain. These observations are made through the precision Bruning-Seigle otoscope. In all my own cases these observations have been made, in addition to the recording of the usual data from otological examinations.

In cases which present most of the factors usually recognized as comprising the classical picture designated clinically as otosclerosis, the external auditory meatus is wider than usual, the skin thin and atrophic in appearance with little subcutaneous tissue apparent, cerumen absent, and the posterior superior segment of the drum moves most readily while the rest of it does not. The drum is thin, almost transparent in spots, and the vascular reflex is sluggish or absent unless prolonged efforts are made to evoke it, when it can be produced. The movements of the ossicular chain are generally impeded, although under negative atmospheric pressure in the external auditory canal the excursion outward of the upper segment (above the short process) of the malleus is possible.

Regarding the postulates of Holmgren and reviewing my own case histories as applied to them, I must note in passing a contradiction in

the fact that Sourdille seeks to submit to the operation patients who present a wide and straight external auditory canal, with a large middle ear which is vascularized and resistant.

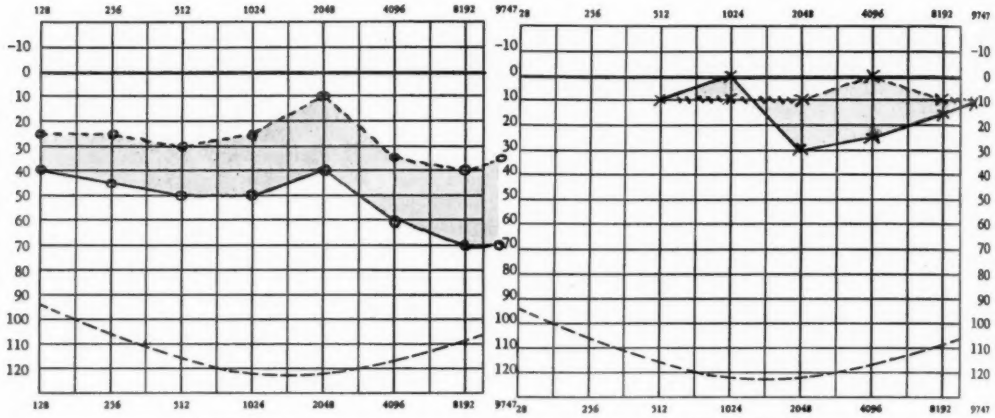
Roentgenography thus far has not been helpful in adding either diagnostic data or criteria useful in selecting cases for surgery. It has given me in each of my cases aid in studying the gross bone structure to determine the presence or absence of pneumatization and the type of cell structure which is present in the given case. Perhaps when the results of planographic studies of the labyrinthine capsule and the middle ear are completed, reports may become helpful in fixing pre-operative data valuable in selecting cases suitable for operation. Sourdille uses stereographic roentgen examinations in his efforts to select his cases. He prefers the type in which the zygoma wall does not pass beyond a vertical plane through the posterior border of the condyle of the mandible.

In my own patients, I have had all types of temporal bones to deal with: large pneumatized bone, the infantile type of small celled bone, and also the sclerotic type. In most instances, both in the material upon which I operated and also in that routinely examined by roentgen-ray in the clinic, pneumatized bone has been predominant.

The stricter the standards observed to set data for the diagnosis of otosclerosis, the less material seems available to subject to operation upon such a diagnosis. The healthy skepticism exhibited by Holmgren in his statement concerning Sourdille's report illustrates this point. "I am skeptical when I read of a patient who could (only) hear loud voice near the concha before operation, and at 60 to 150 centimeters after operation, especially when the author considers that hearing has become 60 to 100 (why not just as well 150?) times improved." I, too, am skeptical of the kind of material selected for this type of surgery, when I fail to find that detailed audiometric and fork tests have been recorded numerous times both before and after operation. My skepticism is increased when I read of vast numbers of patients who have had this operation since from a pool comprising my clinical material and my private practice amounting to over a thousand deafened patients I was only able to find about 25 cases during the period from December 1, 1937 to September 1, 1940—the period during which most of the many cases reported in the literature were diagnosed and the operation performed.

SURGICAL RESULTS

I shall make no attempt to summarize the cases in which patients have been subjected to operation, nor to tabulate successes and failures I have already alluded to the difficulties of making such estimates of success in an evaluation of this type of surgery. The cases reported come from differing clinical categories and results are due to the application of different surgical procedures. All the patients have one factor in common—they are deaf. Some may have had otosclerosis. I am sure not all of them did. In all patients, fenestration of the labyrinthine capsule through operation on the horizontal semicircular canal has been done. The case may be regarded as having a successful outcome if the fenestration has remained open. *That is a surgical success.* We also must record whether the functional hearing has been sufficiently improved to be of practical value. *If both are accomplished the case has reacted favorably to surgical therapy.* We should avoid comparing one surgeon's results with those of another, as each of them is performing a different procedure, probably upon patients differently selected. Not even my own cases should be added together to be tabulated as successes or as failures as far as a given surgical procedure is concerned because I am still "sampling" clinical material and submitting different clinical types of cases to different types of surgery in an endeavor to find the minimal surgical endeavor necessary to improve hearing acuity practically. Manifestly, those cases in which I have left the tympanic structures untouched at this time should not be compared with the ones in which these structures have been surgically disturbed. The end-results of two stage operations by the Sourdille technique cannot be computed with those of one stage operations of a different type. These differing techniques should not be compared until at least enough of them have been done to permit an estimate for each group. Until then only are comparisons possible between one group and another. Such basic surgical studies demand time, careful selection of suitable material, and meticulous bedside and postoperative observations. The literary essays, written by men not actually engaged in doing this type of surgery, add little to our knowledge by the sketchy outlines of cases rather than the detailed reports of case histories themselves. These essays consist principally of compilations of large numbers of cases, in all of which the same thing has been done over and over again, and of a tabulation of the successes and failures taken haphazardly without specifically giving in detail the criteria of selection or the most exact diagnosis possible of the cases. In these reports and essays I see little effort to find the factors which are causing the repeated failures.



Air conduction. Bone conduction.

Fig. 1. Record of the improved hearing acuity in a radical mastoidectomy done 20 years ago. Fenestration done on December 8, 1938. The improvement was present both for air and bone conduction (masked). It lasted 5 months, then the fistula test became negative, and hearing returned to status quo ante operationem.

Adding up the successes for a given surgical procedure may be practical from the standpoint of private practice, but it hardly rates serious consideration on our part as a scientific contribution toward the advancement of our knowledge.

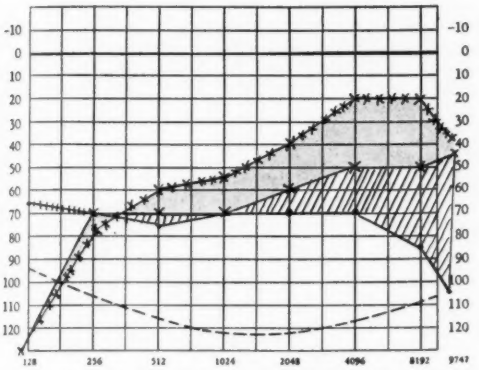
I have followed the reports of all these surgical endeavors since they began to be published. One could wish that some of them had had the benefit of editorial supervision to prevent 2-A audiometric records being placed in comparison with those made on 6-A audiometers! Additionally, the stress in our current American literature and, for that matter, also in the presentations before our scientific assemblies is to a great extent not concerned with even a beginning of a discussion of the many questions at issue, but seems to be designed and specifically arranged in an attempt universally to teach a specific surgical technique *whose value has not been unequivocally established.* Lempert, a protagonist in this endeavor, is even now ranging far afield from his own advocated procedures, in seeking answers to the problems which 21 of his patients present whose fistulas are still open but who have had no improvement in hearing. He likewise is seeking the *whys* and *wherefores* of the bad results in 20 other cases among the 120 he recently reported. These 41 cases (of the 120) had the benefit of his technique and skill. Were Utopian results obtainable by the meticulous adherence to the detailed minutiae of his technique, 120 consecutive successes should have followed the operation in his hands. The factual record, however, tells a different story.

PERSONAL CASES UNDER OBSERVATION

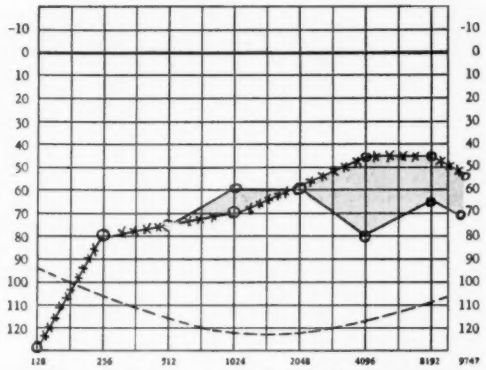
To date I have accepted, studied, and operated on 26 patients, performing different operations on them. One patient had both ears operated upon, thus making 27 operations in all. These cases are divided into the following groups:

	No. operations
1. Radical mastoidectomy, subsequently fenestrated	1
2. First stage, Sourdille operation (cases not yet finished)	2
3. Second stage (completed Sourdille operations)	2
4. One stage, with tympanic cavity and structures untouched	2
5. One stage, epitympanic space obliterated, head of malleus amputated and incus removed	2
6. One stage, epitympanic space obliterated, head of malleus amputated; incus intact	18
Total	27

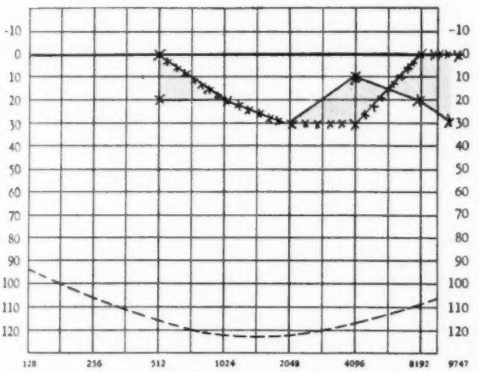
All operations were performed through the postauricular route, and in all the horizontal semicircular canal was fenestrated. It is important to record here for the purposes of this paper what happened to the fenestration in these different techniques. One of the Sourdille procedures is a success from both the practical and the audiometric standpoint. The time element in this case since the completion of the final phase of the Sourdille is 18 months. Figure 2 is the audiometric record of this case to date of this report; and Figure 3 is the photostatic record of the detailed examinations made for each frequency cycle over the whole period of observation. The study of the bone conduction gives interesting data (Fig. 4).



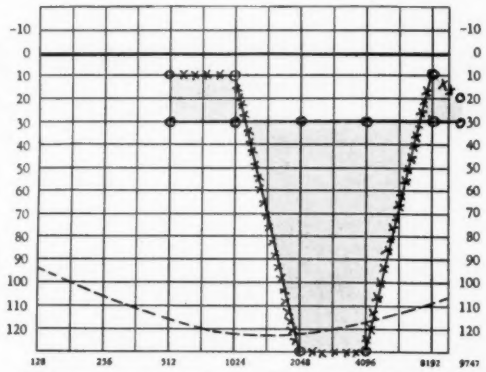
Left ear, not operated upon. Shaded section denotes decibel change since operation, second stage. Starred line indicates postoperative, second stage, curve. At second stage operation, the epidermis was elevated over the horizontal semicircular canal, fenestration performed, and the flap replaced. The fistula remained open during record covering period from December 1937 to August, 1940.



Right ear, not operated upon. The shaded section denotes decibel change since operation, second stage. The starred line indicates postoperative curve.



Left ear, side operated upon. Bone conduction, masked. The shaded section denotes decibel change since operation. The starred line denotes postoperative curve.



Right ear, not operated upon. Bone conduction, masked. The shaded section denotes decibel change since operation. Starred line denotes postoperative curve.

Fig. 2. Case of Mrs. M. C., aged 45. Conventional audiometric charts, showing gain in hearing. The solid line indicates hearing acuity before the second stage of the Sourdille operation. The starred line indicates the last test of hearing acuity. The shaded section below the solid line indicates the level of hearing some time after the first stage. The hearing is improved, in spite of an island of deafness by bone conduction, taken under conditions of masking, with 30 decibels of masking, of same tone as one used in tested ear. The record of conversational losses were, December, 1937, right 58 per cent, left 56 per cent; August 1940, right 55 per cent, left 41 per cent.

The other completed Sourdille was a failure. The second Sourdille operation which failed in my opinion although there is an improvement in the conversational ranges, occurred in a sclerosed type of bone and with a small true cholesteatoma, discovered in the epitympanic space at operation. One of the patients in whom the tympanic structures were left untouched not only has an open reacting fistula 22 months after operation but has hearing sufficiently improved to satisfy the patient. From my objective observations of his audiometric, fork, and voice tests, I would not list the case as a success. The second patient in this group has an open actively reacting fistula after a 19 months' interval of time. The hearing acuity varies with the onset and cession of allergic attacks. Here too there has been improvement in hearing acuity but I do not consider this case a

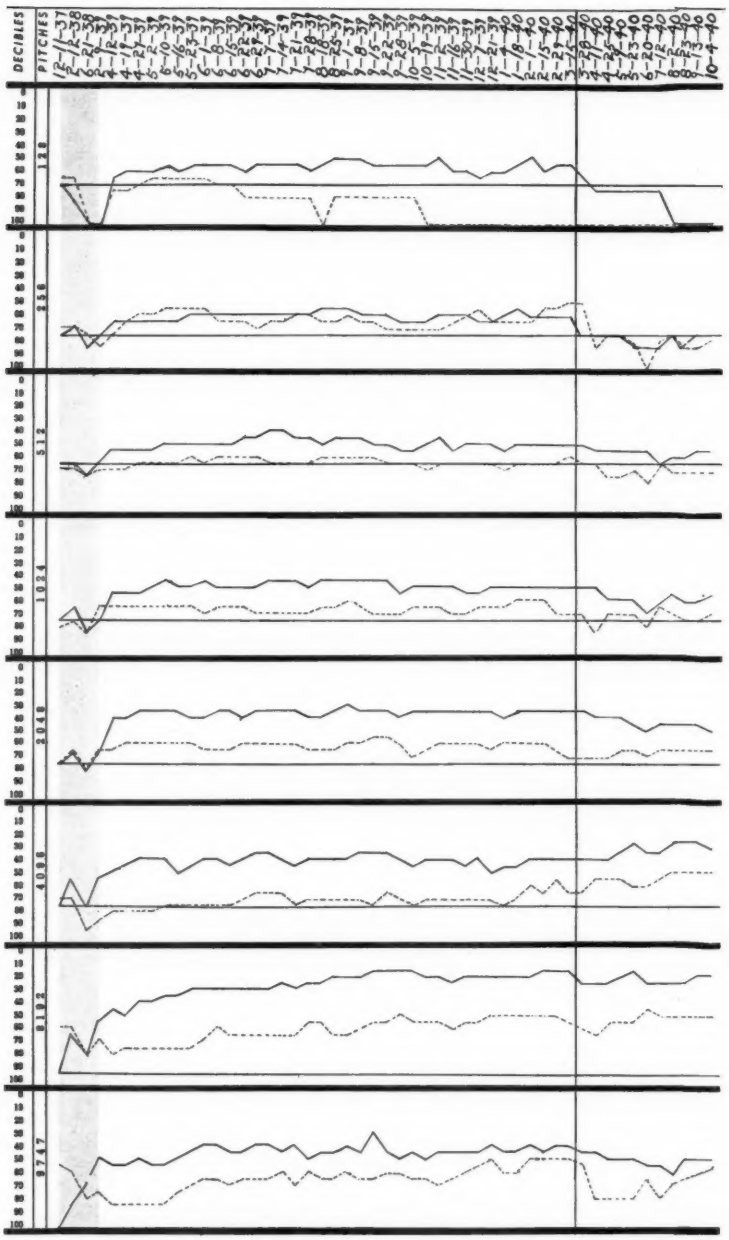


Fig. 3. Case of Mrs. M. C., aged 45 years, date of operation, March 30, 1939. Serial record of audiometric tests for air conduction. Shaded area is interval between first and second stage of Sourdille operation. Vertical line indicates change from 6-A to 6-B Western Electric audiometer. There are 49 tests recorded. Closed line indicates ear operated upon; interrupted line ear not operated upon.

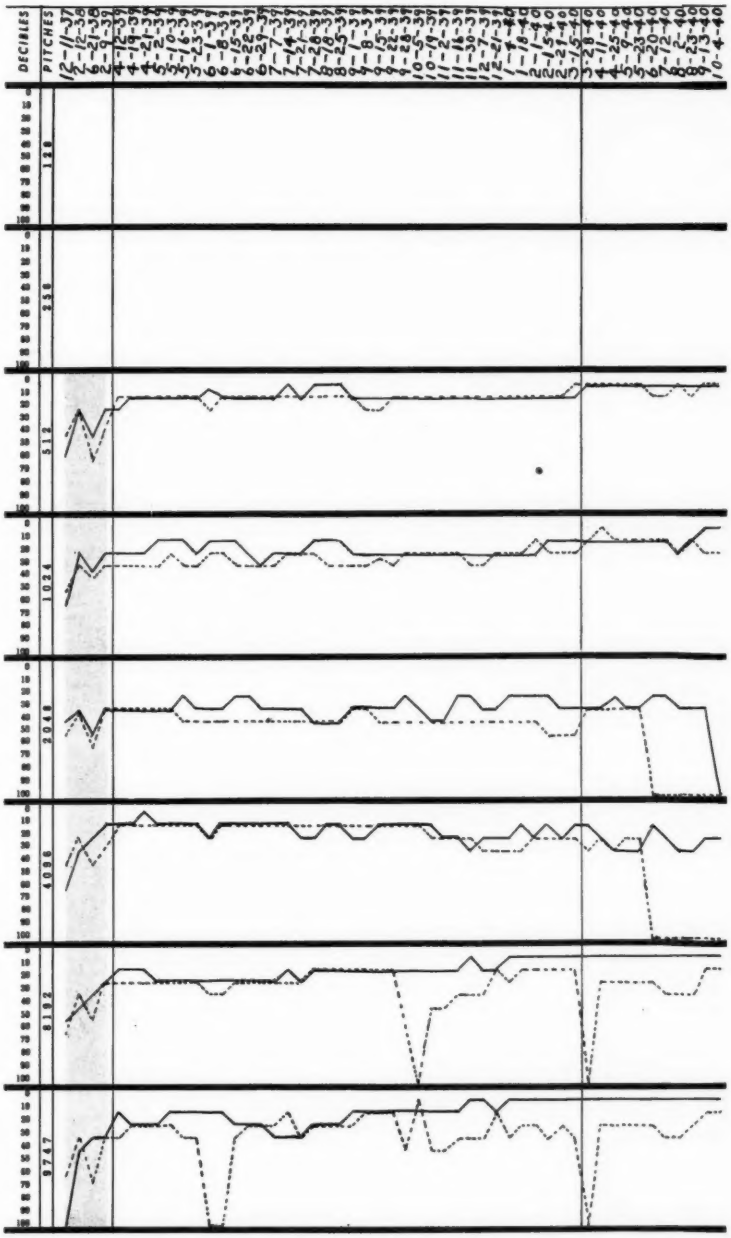
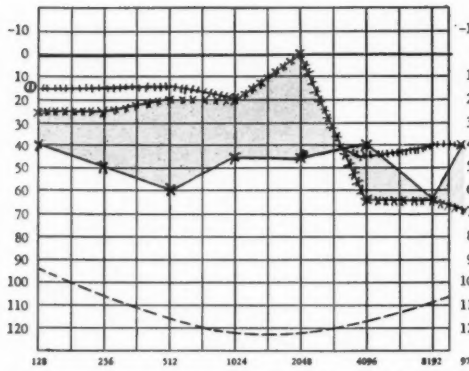
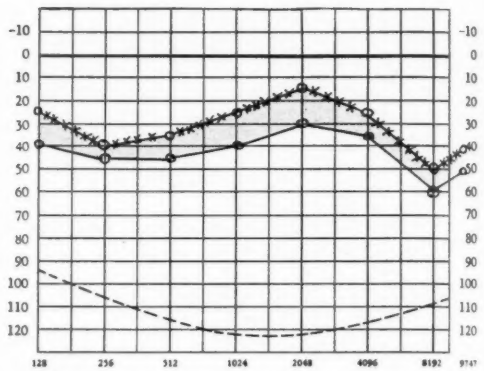


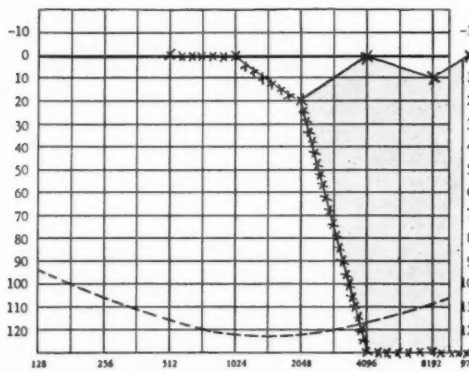
Fig. 4. Same case as in Figures 2 and 3. Serial record of audiometric tests for bone conduction (masked). The dips in bone conduction seem to last about 2 weeks, to be followed by the reappearance of the lost frequency cycle. Repeated tests reveal that the finding is not accidental. The vertical line after March 15, 1940 marks the change from a 6-A to a 6-B Western Electric audiometer.



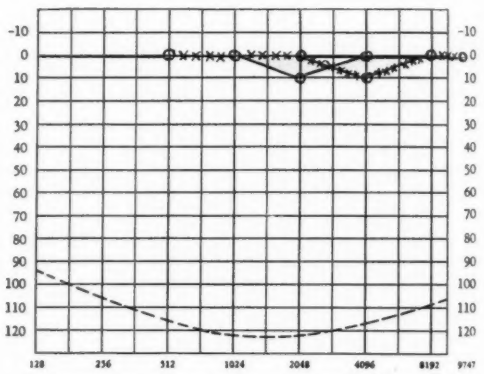
Left ear, operated upon. Shaded section denotes decibel change since operation. Starred line indicates postoperative curve. Fenestration was performed and incus was removed in one stage procedure. Record covers period from February 1939 to September 1940. *1* indicates level of best hearing.



Right ear, not operated upon. Shaded section denotes decibel gain since operation. Starred line indicates postoperative curve.



Left ear, operated upon. Bone conduction, masked. Shaded section denotes decibel change since operation; starred line denotes postoperative curve.



Right ear, not operated upon. Bone conduction masked. Shaded section denotes decibel change since operation. Starred line indicates postoperative curve.

Fig. 5. Mrs. L. F., aged 47 years. One stage, postauricular approach. Note loss in bone conduction for upper ranges of tone. Before blood dyscrasia developed the hearing acuity was better as shown in broken line at *1*. The blood condition is improving, and patient reports hearing improvement. Record of conversational losses, February 1939, right 31 per cent, left 40 per cent; September 1940, right 15 per cent, left 7 per cent.

successful one. Of the 2 cases in which the epitympanic space was obliterated, head of the malleus amputated, and the incus removed followed by fenestration of the horizontal semicircular canal, one case turned out to be a failure, the fistula closed and the hearing acuity did not improve. The other case of this group is a success from every standpoint. The patient had used a hearing aid for many years, is now much improved, and the fenestra is reacting strongly after an interval of 20 months.

Figure 5 herewith presented is the audiometric record of this case. There was a period when the hearing was slightly better than the audiometric record now shows. This is indicated by the broken line on the audiogram. During recent months, this patient has developed a leucopenia, the causation of which is still obscure. The onset of this blood dyscrasia coincides with the drop in hearing acuity. Figure 6 is a photostatic copy of the study in hearing acuity during the whole period. On the bone conduction audiogram

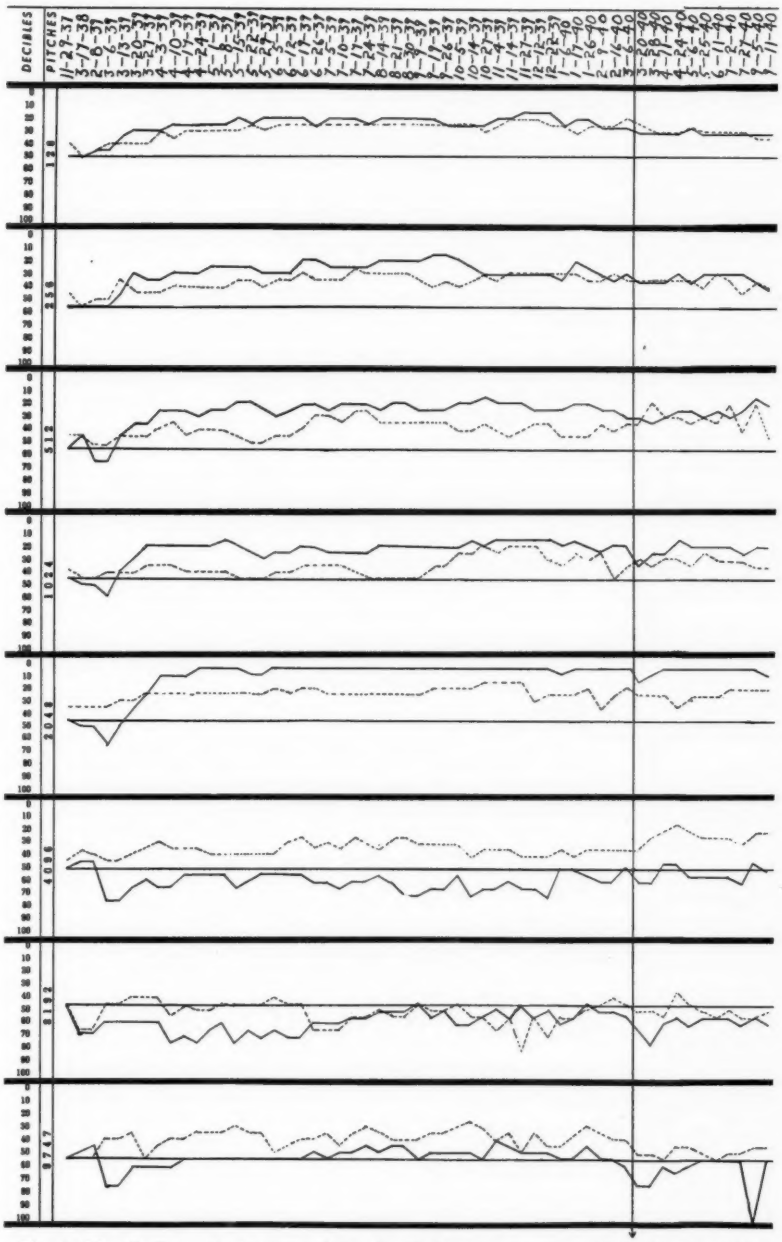


Fig. 6. Mrs. L. F., aged 48 years. Operation, February 23, 1939. Work chart, recording hearing acuity over a period from November 29, 1937, to September 11, 1940. There are 55 tests recorded. The vertical line indicates a change from a 6-A to 6-B Western Electric audiometer. Closed line, ear operated upon; interrupted line, ear not operated upon.

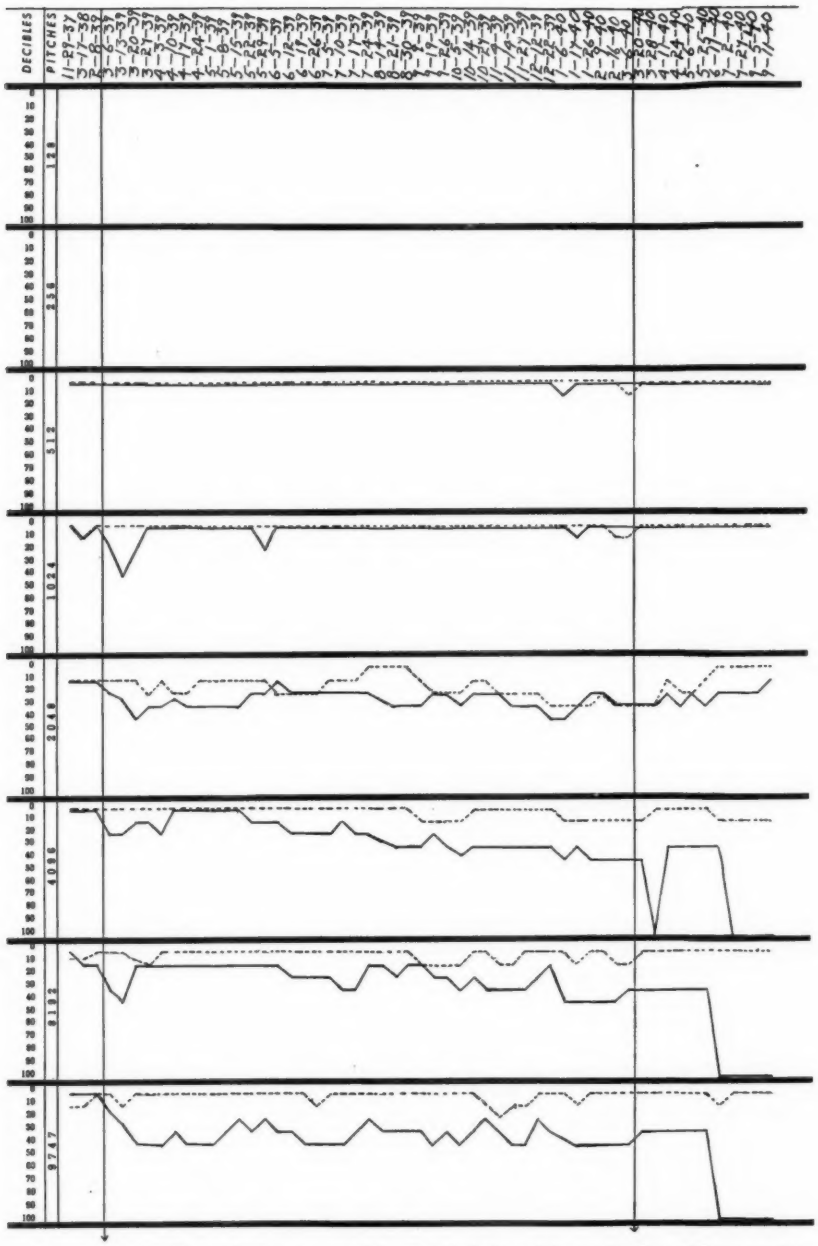
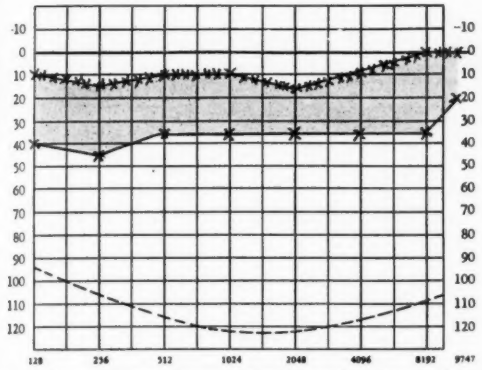
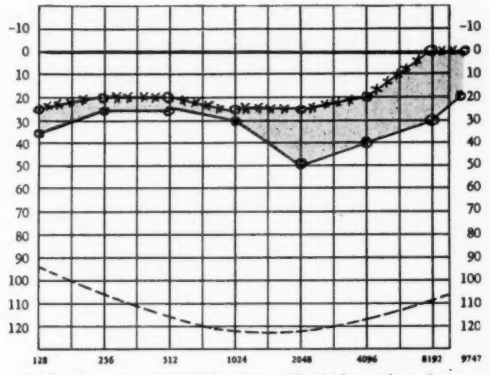


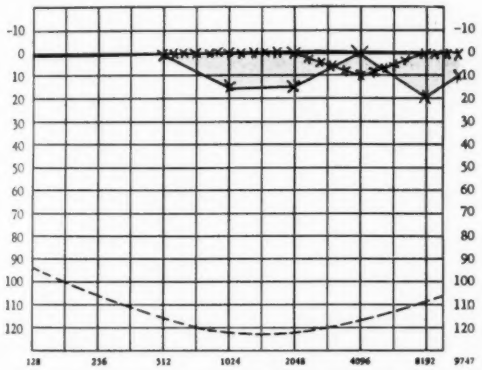
Fig. 7. Same patient as in Figures 5 and 6. Chart of the serial examinations of bone conduction (masked). Change from a 6-A to 6-B Western Electric audiometer on March 6, 1940. Dips in bone conduction and subsequent recoveries are unclarified. They are not accidental findings as on days recorded repetition of tests brought same results. Line between February 8 and March 6, 1939, indicates operation. Closed line, operated upon ear; unoperated upon ear, interrupted line.



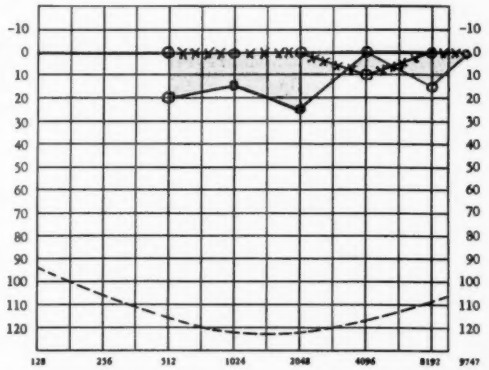
Right ear, operated upon. Shaded section denotes decibel gain since operation. Starred line indicates postoperative curve.



Left ear, not operated upon. Shaded section denotes decibel gain since operation. Starred line indicates postoperative curve.



Right ear, operated upon. Bone conduction, masked. Shaded section denotes decibel change since operation. Starred line denotes postoperative curve.



Left ear, not operated upon. Bone conduction, masked. Shaded section denotes decibel change since operation. Starred line denotes postoperative curve.

Fig. 8. Miss R. G., aged 24 years. Conventional audiometric charts; shaded section shows decibel gain in both ears.

Record of conversational losses, October 1938, right 28 per cent, left 28 per cent; July 1940, right, 9 per cent, left, 19 per cent.

Fenestration of right ear was done and a flap was placed over it. The head of the malleus was removed. For 15 days the flap remained *in situ*. On November 25, 1938, the flap over the fenestration sloughed off. No subsequent covering by flap was done. Record from October, 1938, to July, 1940. Fistula was still open, July, 1940.

(Fig. 7) there appear periodically sharp losses in masked bone conduction. Why these occur is not yet clarified. They are not accidental findings because repeated examinations made during these periods always gave similar graphs. Among the 18 operations, all done through the postauricular route, the epitympanic space obliterated, the head of the malleus amputated, the incus kept intact and *in situ* and the horizontal semicircular canal fenestrated, only a very few were sufficiently functionally improved to be listed by me as successful cases. The interval of time since operation is not, in my opinion, sufficient to estimate even the successes. Some of the fistulas are open, with no improved hearing. I shall, of course, report these cases in detail upon another occasion. Here I desire to present the pertinent details of one of these cases which is still a complete success from every standpoint. This is a patient on whom I operated, obliterated the epitympanic space, amputated the head of the malleus, kept the incus intact and *in situ*, and then fenestrated the horizontal semicircular canal. I called attention to this case in my preliminary report because,

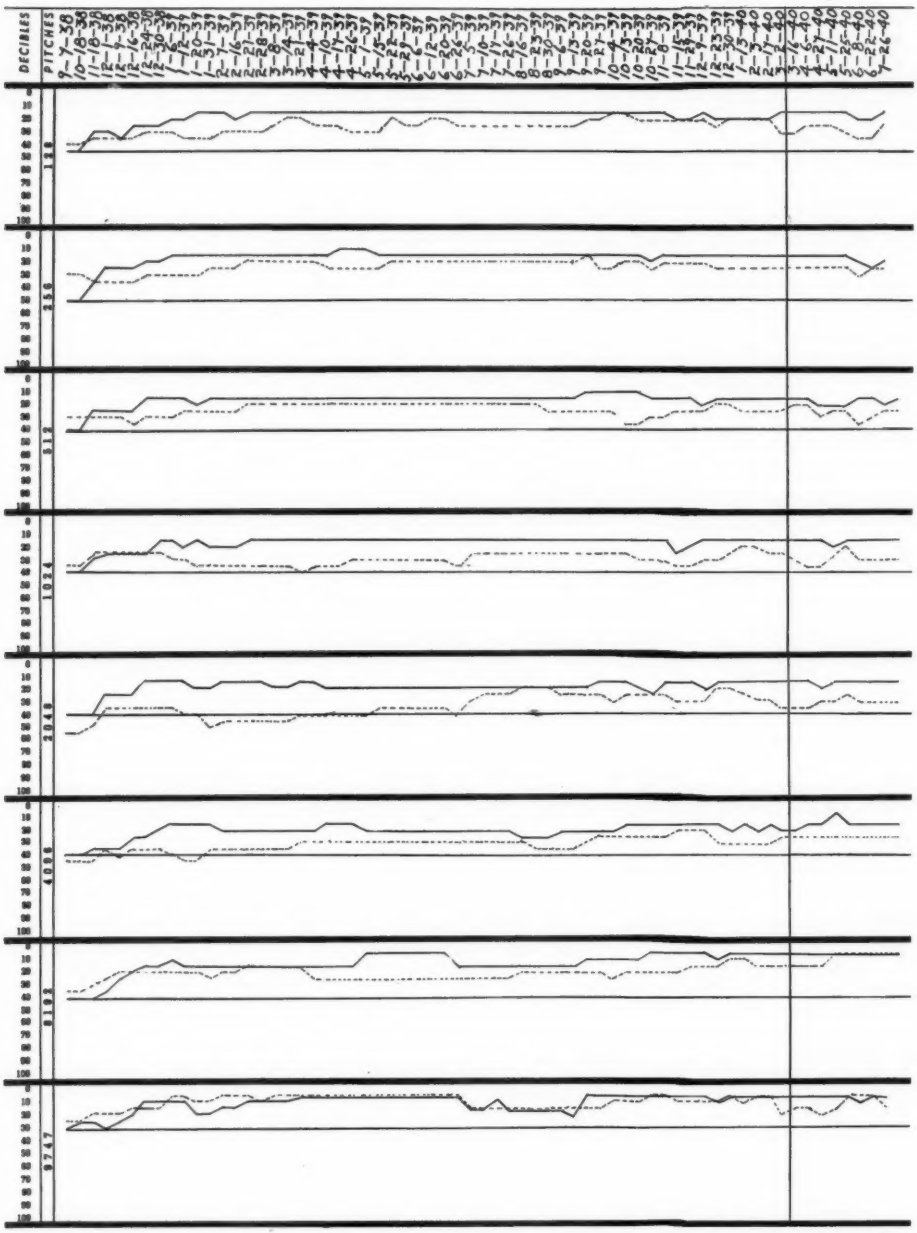


Fig. 9. Miss R. G. Aged 24 years. Operated upon November 8, 1938. Serial audiometric record, showing 64 tests, from September 7, 1938 to July 26, 1940. The vertical line indicates change from 6-A to 6-B Western Electric audiometer. A striking parallelism is shown in improved hearing acuity in the ear (broken line) not operated upon.

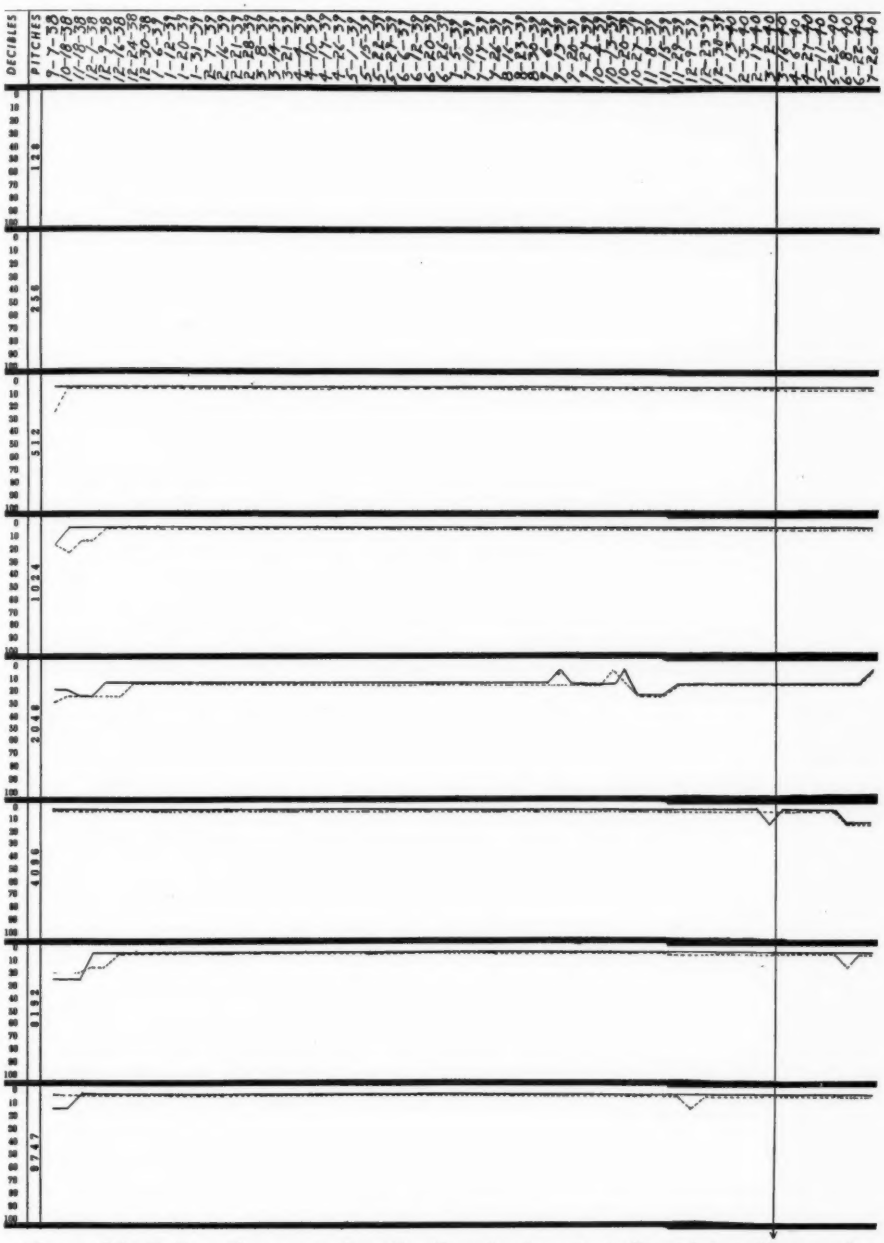


Fig. 10. Miss R. G., aged 24 years. Operation November 8, 1938. Audiometric test of bone conduction (masked). It was good at beginning and has remained so. Vertical line indicates change from 6-A to 6-B Western Electric audiometer.

after a very short interval of time, the flap covering the fenestra sloughed off. For many months, I kept granulation tissues from growing over the fenestra. After 8 months, when only this area was bare, the rest of the wound healed and dry, I permitted the healing to proceed and the coverage of the fenestra became complete. The actively reacting fistula test lessened, upon touch, but is still to be elicited by the Seigle otoscope. The hearing acuity has continued excellent. Figure 8 is the audiometric record of this case to date of this paper. Figure 9 and Figure 10 are photostatic copies of the working charts for the detailed observation of the audiograms of the hearing acuity for each frequency cycle in the scale. The interval of time since operation is 23 months.

CONCLUSIONS

In all the patients operated on, the cover of the fenestra has differed, yet closure of the fistula ensued in many but stayed open in some. Had it stayed open always with a given technique and closed with others, I would have discarded all but the technique which always brought success. Unfortunately this could not be done because successes were as scattered as were the failures regardless of the different technical procedures. The majority of the fistulas closed. Yet the ones remaining open seem to substantiate Canfield's and also Guggenheim's experimental results and conclusions, that the closure is less dependent upon the cover material than upon factors and elements inherently present in the bone itself. *The conclusion is inevitable, that up to the present no sure way has been devised to make the fenestra and reasonably to expect that it will remain open permanently.*

The successes I have been able to procure in the small amount of clinical material available to me for subjection to operation have been obtained in spite of the different technical procedures performed. *The conclusion* is therefore warranted *that factors and elements having nothing whatsoever to do with the cover tissue or with a specific technique* are responsible for the results obtained.

From the manner in which the patients react to the surgery and the end-results from exactly similar technical procedures, with similar audiometric findings, and the usual case histories and otoscopic findings, it is evident *that systemic conditions, endocrine and metabolic dysfunctions play a part not only in causing the deafness* but in continuing it after fenestration. As a corollary, from the observation of the various postoperative periods, the *conclusion seems logical that the cases fall into different categories*, the exact recognition and diagnosis of which is not possible at this stage of our knowledge.

Observations of the patients, who have had successful fenestrations and whose hearing from tests by voice, forks, and audiometric tests is sufficiently good to be classified as successful and for whom a sufficient interval of time has elapsed since operation, present another factor that needs notation. As the patient emerges from the operation period, the vertigo and nystagmus subsides and he is sharply conscious of hearing many sounds of which he was unaware prior to operation. These patients are exceedingly anxious to be cured of their deafness. They spend many hours daily continuously and continually testing themselves. Their family and circle of friends all help in this. After a few months have passed, this awakened interest passes. The newness of the increased hearing acuity has worn off. The patients themselves forget how badly they were handicapped prior to operation. So it is no surprise to have some of these patients appear months after operation, showing an open, actively reacting fistula with a very satisfactory audiogram of hearing acuity with a maintenance of the gained hearing, yet dissatisfied because they still are not hearing normally, and they miss words at the theater or in the general cross conversations in social gatherings. In some, this induces a psychotic phase, enhanced by a phobia of a recurrence of the deafness. I have observed this tendency in both educated and uneducated patients. The conclusion therefore seems inevitable *that the greatest possible care must be exercised in making promises of what will be accomplished by these operations.* Many troublesome annoying experiences will be avoided if not only the patient but his family are told exactly what this surgery holds out for him *and that it is impossible truthfully to predict results on hearing acuity.* In many instances I have put this uncertainty in writing to the patient before accepting him as a subject for operation.

Mr. Hall summed the whole matter up rather neatly at a meeting of the Section of Otology of the Royal Society of Medicine in London when he said, "as long as the patient was fully aware of the nature of the operation, and the chances of improvement, the question of the justifiability (of the operation) did not enter into the matter more than into any other attempt to advance the science of surgery."

At present, within the framework of recorded experiences with this type of surgery and from my own work in this field, *it is impossible to make a definite estimate of its value* to the patient as a

means to restore hearing in a person suffering from progressive deafness of the conductive type. Good results are on record. The exact determination of what type of case will react best upon being subjected to this surgery is still unclarified. The question of what kind of technique will produce the best results in the shortest time with the least danger to the patient is still unsolved. Inherently this surgery, undertaken with the wonted regard for asepsis and a knowledge of the surgical anatomy embraced in the technique, carries little danger to life and only a slight degree of risk to the labyrinthine structures. The risks to the membranous labyrinth, with a resultant further loss of hearing, are definitely increased by reoperations upon the horizontal semicircular canal in cases in which the first fenestration turned out to be a failure. The implantation of pavement epithelium buried from the external air is to be avoided lest pseudocholesteatomas develop.

This type of surgery should be continued with all safeguards and cautions. There is promise in the advancement of the science of surgery in the evolution of this surgical therapy for the deafened.

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GLAUCOMA SURGERY DURING THE PAST TEN YEARS

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IN the management of primary glaucoma the trend is more and more toward earlier operation when indicated. Unfortunately, however, there is still considerable procrastination on the part of many patients and ophthalmologists, and this is to be regretted in view of the better results obtained from operations on early cases as compared with the results with late cases. In a series of 141 eyes operated upon, 90 per cent of the early[1] cases, 51 eyes, showed arrested disease after an average follow-up period of approximately 5 years from operation. Of the late cases, 90 eyes, only 28 per cent showed arrested disease after an average follow-up period of over 5 years from the operation.

In 43 per cent of the advanced cases in this series, the field changes continued to progress in spite of the fact that the operation was successful in reducing the intra-ocular pressure to normal over the 5-year follow-up period. This would indicate that if the vascular process occasioned in the retinal vessels by the increased intra-ocular pressure producing the field changes has progressed to a certain point, or has gathered a certain momentum so to speak, it continues to progress, thus producing progressive field defects in spite of normal intra-ocular pressure. There can be small hope, therefore, for an operative panacea for primary glaucoma so long as operation is deferred until this vascular process has gathered sufficient momentum to progress regardless of the successful reduction of the intra-ocular pressure.

Conceding that the goal of all glaucoma operations is permanently to reduce the intra-ocular pressure to normal, but bearing in mind that this goal may be attained to no avail if the operation has been deferred too long, we shall proceed with a discussion of trends in operative technique during the past 10 years. These have been largely in the nature of modifications and combinations of our standard procedures (iridectomy, iridectomy with sclerectomy, trephine, cyclodialysis, and iris inclusion). It is well to bear in mind that these standard procedures when employed early in the course of the disease in the indicated cases are highly satisfactory in the large majority of instances.

In presenting relatively new techniques very little emphasis will be laid on the statistical claims of their sponsors. In view of the difference in the tractability of the disease to treatment between its early and its late stages, such figures would appear to have little value unless the stage of the disease at which the operation was performed were also known. Clearly it would be unfair to compare the results of one operation done in the early stage with the results of another done when the glaucoma was absolute. The new procedures are usually used sporadically, frequently on advanced cases as secondary or tertiary operations, and are often reported in small series which have not been followed up adequately. Such series are not to be compared with the large series available in which long tried techniques have been carried out in the presence of early as well as advanced conditions and which have been followed over a period of years.

Although ophthalmologists agree that an iridectomy is the operation of choice in acute glaucoma and that the other procedures are contra-indicated unless, perhaps, an iris inclusion can be performed during an interval free of tension, opinion regarding other indications for the use of the various operative techniques is so divided that it is impossible to generalize with regard to it. Any tendency toward unanimity of opinion in this matter which appears to have developed in recent years, however, will be noted.

OPERATIVE TECHNIQUES AND MODIFICATIONS

In the fistulizing operations there has been an effort to secure better filtering areas by having a minimum of adhesion between the conjunctiva and the underlying tissue; thus a more diffuse and flatter bed is secured and also thicker covering of the filtering area as a protection against ectogenous infection. Contributions to this end have been made by Benedict, Gifford, Berens, and MacMillan.

Benedict advocates a method of dissecting the conjunctival flap which he believes assures a

[1]Early cases were considered those in which the peripheral fields had not contracted to a point closer than 30 degrees of fixation in any meridian and in which the blind spots were not larger then 15 degrees in any diameter. All others were considered advanced cases.

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diffuse, generous, subconjunctival filtration of aqueous, thus avoiding the small, localized, elevated, thinly covered filtering bleb or the flat conjunctival bed with no filtration. He claims that the space between Tenon's capsule and the sclera is a confined, limited one but that the space between the conjunctiva and Tenon's is potentially large and thus the desirable one for filtration. His dissection, therefore, is not subconjunctival but subcapsular in order to avoid adhesions between the conjunctiva and the capsule. This is carried down to within 3 millimeters of the limbus, where Tenon's capsule ends, and from this point to the limbus the conjunctiva is dissected from the underlying sclera just sufficiently to reach the limbus over a wide enough area to permit the placing of the trephine blade.

Gifford has reported on the advantages of the watertight suture of Foster Moore. This is a running, closely placed, continuous silk suture which closes the conjunctival wound tightly, and when it is used the anterior chamber usually reforms on the operating table. The aqueous filters out under the flap, elevating it diffusely; this prevents union with the underlying sclera and thus prevents adhesion. Gifford also attributes choroidal detachment and the rapid constriction of the field of vision following a fistulizing operation to postoperative hypotony and he claims that this condition is the result of a leaky conjunctival wound which may be prevented by the watertight suture.

Berens has devised a specially grooved spatula which he inserts under the tightly sutured conjunctival flap to direct the nozzle of an anterior chamber irrigator in order to bleb-up the flap with one-half normal saline solution.

MacMillan recommends the injection of air under the conjunctival flap as well as in the anterior chamber at the completion of the trephine operation. He accomplishes this with a fine curved lacrimal syringe needle after having placed a continuous watertight suture. The air disappears in about 1 week.

Trephine. In the past decade very little has been advanced on the trephine operation. Although there is fairly general agreement that the operation is one of the best operations, if not the best, to reduce intra-ocular pressure, surgeons are more and more seeking other techniques which are better tolerated by the eye and therefore incur fewer complications.

The low-grade chronic iritis that sometimes ensues may be due to the incarceration of ciliary processes in the trephine opening but is really no better understood now than formerly.

The hypotony, which may reach serious proportions, may be corrected by a technique employed by Wheeler, as follows: The epithelium is removed over the upper part of the cornea adjacent to the limbus from 10 to 2 o'clock with a curette. The conjunctiva is incised around the limbus over its upper half and dissected up sufficiently to bring a conjunctival flap down over the denuded cornea; the conjunctiva covering the filtering cicatrix may or may not be excised. The flap is then sutured to the conjunctiva and episclera near the limbus in about the horizontal meridian. If too much of the filtering cicatrix is excised, too large a conjunctival flap will have to be brought down and a slight ptosis may result. This operation is quite effective in raising the intra-ocular pressure to the normal range.

Hans Barkan has advised the use of the Shahan thermophore for hypotony following the trephine operation. He applies it to the filtering bleb for 5 to 10 second periods at a temperature of 165 to 170 degrees four times at intervals of several days.

Glaucoma patients with incipient cataractous changes, either in the periphery with no disturbance of vision or encroaching on the pupillary area with visual disturbance, sometimes show a distressing increase in these cataractous changes after correctly performed glaucoma operations have been done. It is generally conceded that this change is more likely to happen after a trephine operation and less likely to follow the iris inclusion operations.

The trephine operation is also more likely to leave the anterior chamber unrestored for an indefinite length of time and cataractous changes may develop even in an eye with no prior lens changes.

Detachment of the choroid is common after a trephine but is often of no importance. Late infections are always possible. The trend is more and more toward the use of the mechanical trephine of Green.

Modified Lagrange operations. Berens has advocated a modified type of Lagrange operation. He dissects a conjunctival flap down to the limbus and shelves the cornea for 1:5 millimeters. With a specially devised broad hollow-ground keratome, an incision is made 1.5 millimeters from the limbus and the wound is enlarged 0.5 millimeters on each side toward the limbus, with scissors. With a specially devised scleral punch the central lip of the wound is serrated. A two-cut iridectomy is done, the iris being torn at its root. The conjunctiva is closed with a watertight continuous suture

and one-half normal saline solution irrigated under the conjunctival flap as described elsewhere.

Lawrence Post advocates a subconjunctival type of incision in performing an iridectomy. The upper half of the conjunctiva is ballooned with an injection of normal saline solution. With a Graefe knife a Lagrange type of incision is made over the upper one fifth of the limbal circumference. The knife emerges under the conjunctiva and is withdrawn without making any more conjunctival opening than the original puncture wound. This is enlarged to 4 millimeters with scissors and the iridectomy is then performed through it.

Spratt dissects down a pocket conjunctival flap, shelves the cornea 1.5 to 2 millimeters, makes a Lagrange type of incision, excises a lip of the sclera, and does an iridodialysis by pushing the iris down with forceps toward the pupillary area.

Curdy dissects down a conjunctival flap and excises an elliptical piece of sclera by starting the incision *ab externo* and completing it with scissors.

Iris inclusion operations. The usual iris inclusion operations consist of the meridional and transverse types of iridencleisis, with modifications of each, and the iridotasis operation. During the past 10 years several modifications of these procedures have been advanced. Herbert advocates the production of an iridodialysis before pulling the iris out for inclusion according to the iridotasis technique. He claims the iridodialysis interferes with the blood supply of the included iris sufficiently to cause it to atrophy and disappear in time after it has served its purpose of causing fistulization, and also that over the fistulizing area the conjunctiva thickens and thereby serves as a better protection. The dialysis abnegates the function of the dilator muscles, thus preventing it from pulling the iris back into the eye. Herbert has also recommended the same type of subconjunctival Lagrange incision for performing an iridotasis as Post has advised for doing an iridectomy.

Greenwood makes a Lagrange incision, excises or punches the scleral lip, does two meridional cuts in the iris, and includes the tongue of iris between these two cuts. The conjunctiva is closed with a watertight suture.

Denig recommends what he terms an iridotorsion operation. The included portion of the iris is curled around a wire so that the pigment epithelium is out, thus forming an epithelial-lined tube of iris tissue extending from within the eye out under the conjunctiva.

Goar and Schultz advocate dissecting a conjunctival flap and making a 6 millimeter incision near the limbus with a keratome *ab externo*. A meridional iridotomy is done and one pillar is flattened out along the scleral surface with the pigment layer exposed. Constantine does a similar procedure but includes both pillars.

Gifford advises an iridencleisis with meridional iridotomy as particularly efficacious for buphthalmos, and Wolfe recommends the use of the same type of procedure combined with a sclerectomy as particularly good in the treatment of glaucoma in aphacic eyes.

A considerable number of surgeons feel that the iris inclusion operations should not be done in cases of congestive glaucoma. Massage after the operation is frequently practiced.

Cyclodialysis. The question of how the cyclodialysis operation functioned was in dispute for some time. Some claimed that it was due to the passage of aqueous from the anterior chamber directly into the suprachoroidal space; others, that freeing of peripheral synechiae at the time of operation was most important; others, that atrophy of the ciliary body, resulting in subnormal aqueous output, was the rationale of the operation.

It has now been definitely established, however, that the operation works because of a fistulous opening from the anterior chamber into the suprachoroidal space. It is also agreed that this fistulous opening tends to close so that the operation leads to a permanent reduction in intra-ocular pressure in only about 20 per cent of unselected cases. Efforts have therefore been directed toward securing a permanent fistulous tract.

Mauksch has tried to accomplish this by what might be called an intra-ocular or a suprachoroidal iridotasis. A technique for ordinary cyclodialysis is carried out except that the scleral opening is made only about 4 millimeters from the limbus and 4 to 5 millimeters wide (Fig. 1a). With slightly curved, delicate forceps the iris is grasped via the cyclodialysis route and pulled backward into the suprachoroidal space but not to the scleral opening (Fig. 1b and c). Mauksch reported on only 4 eyes operated upon by this method; the tension was reduced in 3 but there was only a short follow-up period. The only other report on this operation that I have been able to locate is one by Suker who employed it on 24 eyes in 15 patients. Tension was reduced in 20 eyes followed from 10 days to 10 months. The fact that in 10 years' time there has been no further report, either by the sponsor or others, would seem to indicate that the operation has not proved satisfactory.

Fig. 1

Fig. 1. The Mauksch operation, an intra-ocular or suprachoroidal iridotasis. a, The spatula inserted through the scleral opening and into the anterior chamber severing the scleral spur. b, the forceps inserted through the operative tract and grasping the iris. c, The iris withdrawn into the suprachoroidal space.

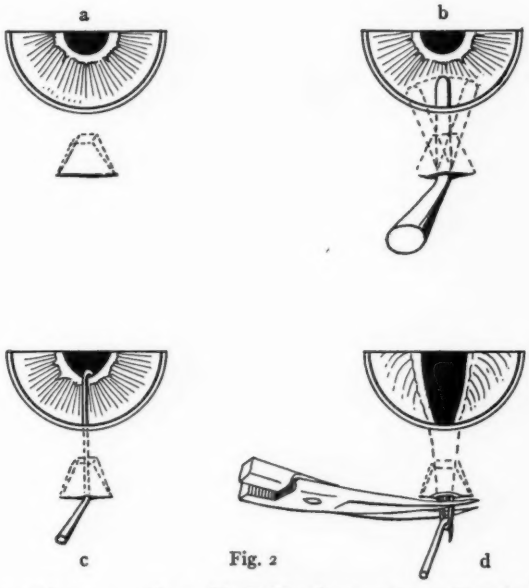

Fig. 2

Fig. 2. The Del Barrio operation. a, The scleral incision made obliquely. b, The spatula inserted through the scleral opening into the anterior chamber severing the scleral spur. c, A blunt hook inserted through the operative tract and engaging the pupillary margin of the iris. d, The iris withdrawn by the hook and part of sphincter portion resected.

Del Barrio has advocated a modification of the Mauksch operation. After dissecting a conjunctival flap he makes a keratome incision obliquely through the sclera 5 millimeters from the limbus at 10:30 o'clock for the right eye and 1:30 o'clock for the left eye. The incision is made quite tangentially, the sclera being traversed over a distance of from 2 to 3 millimeters (Fig. 2a). The internal opening is only just large enough to admit comfortably a spatula which is advanced between the sclera and the ciliary body until it appears in the angle of the anterior chamber (Fig. 2b). The usual cyclodialysis is then done over as wide an area as possible. After the spatula is withdrawn, a small blunt hook is inserted through the same tract, the pupillary margin is engaged, and the iris is withdrawn until it just emerges through the external scleral incision (Fig. 2c). A small piece of the sphincter is excised to prevent the iris from being drawn back inward and the conjunctiva is closed (Fig. 2d). This operation is supposed to have certain advantages over the Mauksch technique. Forceps are not used to grasp the iris and the incision can therefore be smaller and a tendency toward ectasia of the ciliary body avoided. Also injury to the ciliary body is less likely with the hook. The operation had been performed on 39 patients with good results.

Another technique advanced to keep the communication between the anterior chamber and the suprachoroidal space open is that of Troncoso. This consists of the usual cyclodialysis procedure supplemented by the implant of a strip of magnesium. This is done by a specially devised instrument which is inserted through the scleral opening along the tract of the cyclodialysis operation for a short distance into the anterior chamber. The magnesium emits hydrogen gas and disappears in about 20 days. It is nonirritating and the gas prevents a closure of the operative opening as well as the reattachment of the ciliary body

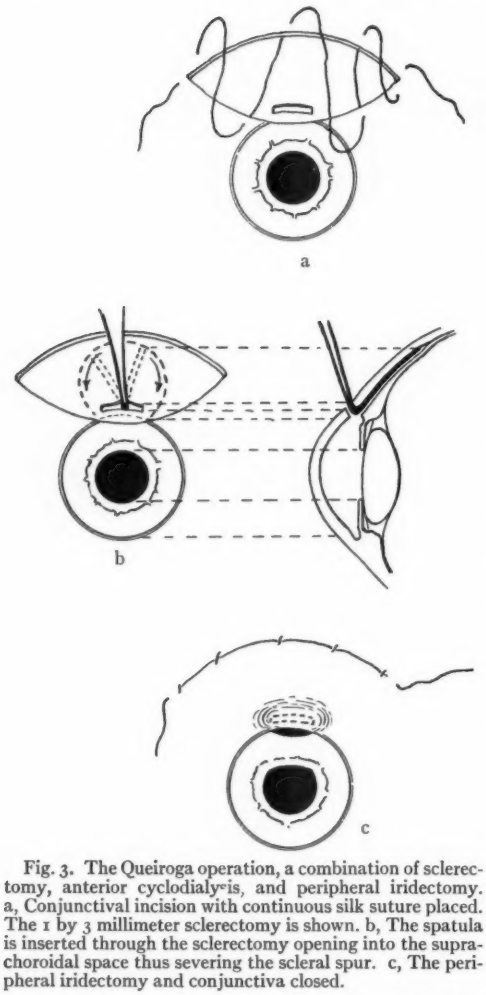

Fig. 3. The Queiroga operation, a combination of sclerectomy, anterior cyclodialysis, and peripheral iridectomy. a, Conjunctival incision with continuous silk suture placed. The 1 by 3 millimeter sclerectomy is shown. b, The spatula is inserted through the sclerectomy opening into the suprachoroidal space thus severing the scleral spur. c, The peripheral iridectomy and conjunctiva closed.

to the sclera. The technique has been studied extensively on animal eyes and employed on 12 human eyes.

Brecher used the membrana testacea, which is the delicate keratogenous membrane just under the shell of an egg, for insertion into the anterior chamber through the tract of the cyclodialysis operation. Only 1 patient had been operated on when the report was made and the follow-up was for a period of only 5 weeks.

A modification of the usual cyclodialysis technique has been advocated by Sallmann. This consists of placing a 1.5 millimeter trephine opening in the sclera 8 millimeters from the limbus instead of making the usual scleral incision. The author claims that with this technique there is less chance of prolapse of the vitreous and injury to the ciliary body. He also believes that there is a passage of aqueous from the anterior chamber through the trephine opening for about 2 weeks and that this helps to keep patent the cyclodialysis opening through the scleral spur.

Gifford proposes certain departures from the usual technique. He gives 100 cubic centimeters of 50 per cent solution of sorbitol intravenously the night before the operation. Sorbitol has advantages over the other hypertonic solutions by virtue of its more prolonged effect and the fact that it can be used safely in diabetes. The scleral incision is made 3 to 4 millimeters long and the anterior lip is punched out with a Holth punch. After the operation a 0.5 per cent solution of physostigmine is instilled with the idea that the miosis will tend to prevent the forming of adhesions of the iris root to the sclera, and that in this manner closure of the cyclodialysis opening will be avoided.

Wheeler has advocated a combination of the cyclodialysis operation with iridectomy. After the cyclodialysis has been performed, a keratome incision is made at the limbus under the conjunctival flap and an iridectomy performed. One of the rationales of this operation is that the cyclodialysis procedure frees any peripheral synechiae present and the iridectomy then removes the iris over this area, and thus opens up the angle for future drainage and also prevents synechiae from re-forming. It seems quite doubtful, however, whether an angle thus opened is ever able to resume drainage. In any case the operation accomplishes one important thing; i.e., the removal of the iris over the area of the cyclodialysis so that it cannot become adherent to the sclera opposite its recessed site which would close the communication between the anterior chamber and the suprachoroidal space.

Lauber approves of the cyclodialysis combined with iridectomy but prefers to perform the iridectomy first. He makes the scleral incision for the cyclodialysis, then the limbic incision, and performs the iridectomy, and then completes the cyclodialysis. Following the trephine operation he sometimes inserts a spatula through the trephine opening and does a cyclodialysis. This is easier to do when a 2 millimeter trephine is used.

Another modification of the cyclodialysis operation is that sponsored by Queiroga. This is a combination of sclerectomy, anterior cyclodialysis, and peripheral iridectomy. The tech-

nique is as follows: After a conjunctival flap is dissected down to the limbus above, two parallel horizontal incisions are made partly through the sclera, 1 millimeter apart, 2 millimeters from the limbus, and approximately 3 millimeters long. One of the scleral incisions is carried deeper than the other until aqueous appears at one point. The sclera is then grasped with fixation forceps and the 1 by 3 millimeter piece of sclera is excised with scissors (Fig. 3a). A spatula, bent almost at right angles, is inserted posteriorly into the filtration angle, through the scleral spur, and into the suprachoroidal space, and is rotated over a distance of 90 degrees (Fig. 3b). If peripheral synechiae are present, the spatula is inserted anteriorly and the synechiae freed. A peripheral basal iridectomy is then performed (Fig. 3c).

This operation is advocated by the author in all types of glaucoma except acute glaucoma and secondary glaucoma from intra-ocular inflammation, or subluxated lens. Twenty-one eyes were operated on and the intra-ocular tension was reduced to normal in every case. Some of the patients were not followed after their discharge from the hospital, others were followed only several weeks, and none was followed longer than several months.

There is fairly general agreement now that the straight cyclodialysis operation is especially indicated in glaucoma secondary to cataract extraction and discission. This has been particularly stressed by Elschnig, Gradle, and Gifford who point out that its effectiveness in this type of glaucoma may be due to the fact that adherent pillars and tags of capsule can be separated from the scar; that, when an iridectomy has been performed, and the spatula is directed especially over the area of the coloboma, the new channel for drainage is more likely to remain open since the iris cannot adhere to the sclera and thus close the new opening; and lastly, that it is the only operation that can be done in this type of case with assurance that vitreous will not be lost. Another reason, however, would seem to be that the aphacic state of the eye minus the zonular pull during accommodative effort, which tends toward less apposition of the ciliary body toward the sclera, predisposes to a patent communication between the anterior chamber and the suprachoroidal space.

In cases of primary glaucoma the operation is indicated more in the chronic, simple type of case in which the tension is relatively low. Any postoperative rise of tension tends to press the ciliary body against the sclera and close the drainage channel.

Seton operations. Two types of Seton operation have been revived. Row does the usual cyclodialysis procedure and then inserts a special grooved spatula through the operative tract and passes through this groove a piece of looped horsehair until the looped end appears in the anterior chamber. The two ends which project from the scleral opening are buried under Tenon's capsule. Wolfe and Blaess advise a conjunctival flap to the limbus down and in, and another down and out. A keratome incision is made into the anterior chamber at the limbus under each flap. A straight blunt-tipped lacrimal needle, threaded with braided white silk, is inserted into the anterior chamber from one incision to the other and the needle is withdrawn, thus leaving the thread extending across the anterior chamber. Each end is cut off 4 to 5 millimeters from the limbus. An advantage claimed for this is that the silk can be manipulated if necessary to restore further drainage. Reitsch dissects down a tongue of sclera 1.5 millimeters by 6 millimeters extending through half the thickness of the sclera and having a fixed base at the limbus. A keratome incision is made and the tongue of sclera is inserted between the lips of the incision and into the anterior chamber. Four patients were operated upon by this method, with good results.

Cyclodiathermy punctures. A new principle in the operative treatment of glaucoma has been advanced by Vogt. He reports on cyclodiathermy punctures which he claims reduce the intraocular tension by lessening the production of aqueous. The operation is performed by a circular incision in the conjunctiva, 4 to 5 millimeters from the limbus, thus exposing the sclera. Sixty to 100 punctures of from ½ to 1 second's duration are made with a diathermy needle 0.5 millimeter long and 0.18 to 0.2 millimeter thick to form a girdle zone extending not closer than 2½ to 3 millimeters from the limbus and extending backward 5 to 6 millimeters from the limbus. The current used should be 60 to 70 milliamperes. There should be good conjunctival closure. The further away from the limbus the punctures are made the less deep they should be and the shorter in duration.

On the grounds that the physiological production of aqueous is too much for a glaucomatous eye, this operation seeks to reduce this production to subnormal by injury to the ciliary body. When the operation has been successfully performed even the use of homatropine and atropine fails to produce a rise in tension. The author admits that the inability to regulate the effects or dose of the operation is a disadvantage.

The complications of the operation, which arise principally as a result of making the punctures too close to the limbus and of not having the needle the proper size, are as follows: (1) marginal keratitis which occasionally progresses to ulceration; (2) cataract which is particularly prone to develop if incipient changes were already present; (3) iritis with posterior synechiae; and (4) iris and anterior chamber hemorrhage which may appear as late as 8 to 14 days postoperatively.

Vogt feels that the operation is not a serious competitor of the customary procedures for increasing the aqueous outflow because of the tendency to complications. It is to be used primarily when other methods have failed, particularly in the following types of cases: (1) total and long standing absence of the anterior chamber, especially in those cases in which the anterior chamber fails to re-form and the tension remains elevated after an operation; the author reports on the results of this technique in 5 such patients: the tension was reduced to normal and the anterior chamber re-formed; (2) glaucoma in aphacic eyes, especially when there is vitreous in the anterior chamber; (3) glaucoma with cataract, in preparation for the cataract extraction; (4) hemorrhagic glaucoma; and (5) iridocyclitis with secondary glaucoma. The inclusion of this last type is surprising but Vogt has performed this operation on several such patients with resultant normalization of the tension; most amazing of all, the corneal precipitates disappeared.

Lloyd has been successful in reducing intraocular pressure by the application of diathermy heat alone.

Vitreous fistula operation. Lindner has reported an operation designed to produce a vitreous fistula by means of the following technique: At a site down and out, a triangular conjunctival flap is dissected up with the apex at the limbus; 10 millimeters from the limbus a 2 millimeter trephine is done through one-half the scleral thickness, and this portion of the sclera is removed; electrocoagulation is applied to the base and the walls of the trephine opening with the idea of coagulating the adjacent choroid and retina; then a 1½ millimeter trephine opening is made through the base of the former trephine site; the exposed choroid is punctured with a discission needle; a bead of vitreous presents, and, by light pressure on the globe and by sticking the discission needle deeper, another bead presents and is cut away; this should be repeated until fluid vitreous appears; the conjunctiva is then closed.

This operation is indicated in cases of glaucoma with very high tension (80 to 100 Schiötz) and almost no anterior chamber, and in cases in which the anterior chamber does not re-form for a long period following a glaucoma operation. It is a transitory fistulization which contracts the vitreous and re-establishes or deepens the anterior chamber and is to be looked upon only as a rescue measure to make a later operation easier and safer. The author has performed the operation on 50 eyes with only 1 complication. This was a retinal detachment which occurred because of insufficient coagulation and which was later successfully re-attached.

Goniotomy and multiple iridectomies. Otto Barkan divides cases of primary glaucoma into two groups as follows:

1. Deep chamber glaucoma. This is characterized by an anterior chamber of usual depth and by an open filtration angle. The underlying pathology is an obstruction in the sclerocorneal trabeculae which induces a retention glaucoma and suggests for this group the term "trabecular glaucoma." In this group are the cases usually referred to as chronic simple glaucoma, chronic noncongestive glaucoma, and senile glaucoma, and for the early cases he recommends primarily the operation of goniotomy according to the following technique: The operator wears a binocular head loupe. The patient's pupil is previously contracted with eserine. A specially devised contact glass is inserted which affords a magnified view of the interior of the filtration angle. A special goniotomy knife is passed across the anterior chamber and through the optic axis to the opposite angle, and an incision is made in the trabeculae for one-fourth of their circumference. According to the author, this re-establishes the normal direction of outflow from the anterior chamber into the canal.

Goniotomy is advocated in early "trabecular glaucoma" which shows a pigment band over the site of the trabeculae, as seen with the gonioscope, indicating mechanical obstruction. In "trabecular glaucoma" with considerable loss of field vision, or with the constriction close to fixation, Barkan recommends one of the internal or external filtering operations.

2. Shallow chamber glaucoma. This is characterized by a shallow anterior chamber, permeable sclerocorneal trabeculae, and a narrow angle, the temporary closure of which produces transitory rises in pressure. In this group are the cases usually referred to as chronic congestive glaucoma and for them he recommends his technique of multiple peripheral iridectomies, performed through multiple valve-like keratome incision as follows: The anterior chamber is deepened

by the injection of physiological saline solution, preceded usually by a posterior sclerotomy and rarely by aspiration of .5 cubic centimeter of vitreous when the vitreous is of firm consistency or has a very high pressure. Several small oblique valve-like keratome incisions are then made at the limbus. Through each of these a small portion of the root of the iris is excised. The author's claim for this operation is that the iridectomies cause a retroplacement of the iris diaphragm over and adjacent to the operative sites, thereby deepening the anterior chamber and widening the entrance or access to the angle.

Venous communication operation. Some thought has been given to the possibility that a sclerosis of the sclera causing a constriction of the vortex veins and thus an embarrassment of the venous return from the eye might be an etiological factor in primary glaucoma. With this in mind Sondermann has suggested an operation designed to establish a communication between the veins of the uvea and the veins of the conjunctiva. With a special spatula-like knife he makes a canal in the sclera which is 2 to 2½ millimeters wide and extends down to the suprachoroidal space. Into this canal Sondermann inserts a narrow strip of conjunctival tissue.

CONCLUSION

In conclusion, then, it can be said that the trend is more and more toward the early recognition of glaucoma both by the patient and by the doctor. To this end the sight-conservation organizations should make an effort to familiarize the public with the cardinal symptoms of the disease; the doctor should always be glaucoma conscious and detect the disease in its early stages by means of refinements in perimetry, routine use of the tenometer, study of diurnal tension curves, and sometimes by provocative tests. When recognized in its prodromal or early stages it can be treated satisfactorily in a much higher percentage of cases than is possible in later stages, either by nonsurgical means or by surgical measures when these are indicated. Ideally, glaucoma should be treated by removing its underlying cause but until this is possible our hope is to prevent, in so far as possible, its deleterious effects by medication or operation. The struggle continues, therefore, to devise an operative technique that is most likely to reduce the intra-ocular pressure to normal and that predisposes to a minimum of complications. It must always be borne in mind, however, that this goal may be attained to no avail if the operation is performed too late in the course of the disease.

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ADVANCES OF THE PAST TEN YEARS IN RETINAL DETACHMENT SURGERY

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EVERY ophthalmic surgeon is familiar with the thrilling and dramatic story of the evolution of the modern operations for retinal detachment. It is unnecessary now to discuss the cruel, barbaric, hopeless treatment of this condition in the pre-Gonin days. Those who are interested in the historical phase of this subject should read W. E. Krewson's article on the "History of the Surgical Treatment of Retinal Separation," from which I have freely borrowed. One will find here descriptions of scleral puncture, aspiration of subretinal fluid, galvanocautery punctures, discission of the vitreous, longitudinal incisions, sutures of the retina, subconjunctival injections, intra-ocular injections of iodine, electrolysis, Deutschmann's operation and a host of other procedures. The fact that such a vast number of operative measures had been advocated indicates their uselessness.

One should pause here to pay tribute to the man above all others responsible for the modern surgical treatment of retinal detachment. Jules Gonin laid the foundation of his epoch-making discovery of the importance of the tear or hole throughout 17 years of eating, sleeping, and pondering over retinal detachment, as a study of his early writings show. In 1921 he presented his work to a world, which remained skeptical for 8 or 9 years, then followed a deluge of world-wide reports of successful cures of a hitherto practically hopeless condition. This brings us to 10 years ago and the further advances of retinal detachment surgery fall within the scope of this paper. I am reluctant, however, to dismiss Gonin without saying a little more. I had the unforgettable privilege of spending 2 weeks at Lausanne in 1930 and of observing the man and his work. Dynamic, friendly, pink and white, enthusiastic, bubbling and exploding with energy, he laid the wealth of his material and technique before spectators from all over the world, without reservation or stint. His amazing linguistic powers enabled him to explain his ideas in French, German, English, Spanish, Lithuanian, and Portuguese, perhaps other languages too. But one did not need to understand his words; his deeds spoke for themselves. Since then, of course, the tribute of his colleagues and thanks of countless patients everywhere have been heaped upon his memory and will continue to be as long as ophthalmology exists.

On the flyleaf of my copy of his book, published in 1934, he wrote "post pessimissimum spes nova!", a motto which put a period to his work. He died in June, 1935, and was awarded posthumously the von Graefe medal, one of the most cherished prizes in ophthalmology.

The classical Gonin operation has been replaced, at least for the time being and for the most part, by other procedures. This was done because of certain disadvantages of the operation. These are (Duke Elder): (1) the difficulty in accurate localization of the hole, a *sine qua non* of a successful Gonin operation, (2) the necessity of several operations if localization has not been accurate or if several holes exist, (3) the destruction of the surrounding region of the retina, leading to further hole formation, and therefore, to possible recurrences, (4) the danger of postoperative hemorrhage, with the resultant gross diminution of visual recovery, (5) the formation of vitreous bands at a later date involving traction on and tearing of the retina, with a recurrence of the detachment. However, in spite of these disadvantages, an occasional case presents itself in which the Gonin operation may be the one of choice. I refer here to that healthy patient in whom the hole is recent, single, and not too large in a flat detachment, in a favorable location capable of being accurately localized. In this event, it will be found that the trauma and reaction of the operation are slight, and the recovery and convalescence of the patient materially shortened.

Because of the disadvantages and shortcomings of the Gonin operation, especially the necessity of an exact localization of the hole, other operations have been evolved, none of which is completely satisfactory in every case. At the present time we are in a state of fermentation or flux regarding these operations, but as the evolution continues one can prophesy with confidence that the time is not too far distant when one can predict a successful outcome in 90 per cent of the cases.

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Whatever technique has been promoted, the fundamental purpose of the operation is the obliteration or isolation of the tear or holes of the retina. Gonin's chief contribution was the recognition of the fact that single or multiple tears can almost always be found in every case, if searched for long enough, and the cure can only be obtained by sealing it off, by producing an inflammatory adhesive choroiditis.

In the past 10 years then advances in the surgical treatment of retinal detachment have been concerned with the satisfactory solution of the fundamental conditions. These are: (1) the finding of the retinal hole, (2) its localization, (3) its obliteration, (4) the postoperative and convalescent care of the patient.

The finding of the retinal hole. One can do no better, when discussing this topic, than to repeat Duke Elder's words. "The first essential is, then, to find and localize the retinal tear, and this is frequently no easy thing to do. It involves the careful and repeated examination of every part of the fundus under full mydriasis, and since most holes (about 80%) are near the ora, particular attention should be paid to the periphery. Further, since more than one hole frequently exists, the finding of one does not justify the cessation of the search. Small holes in the main part of the fundus are best seen by direct ophthalmoscopy, but, owing to the prismatic effect of the condensing lens, the indirect method allows of easier and fuller access in the extreme periphery. If a hole cannot be seen at a first examination, it may well be hidden by some retinal fold and may be evident after the patient has been kept recumbent for some days, when the configuration of the detachment has changed; or it may be legitimate finally to draw off the interretinal fluid by a syringe with the same end in view.

"With regard to the hole itself, it need not necessarily be found at the site of the detachment at the time of the examination, for, particularly if the hole is in the upper part of the retina, the interretinal fluid may have drained away by gravity to the lower quadrants of the globe, inducing an inferior detachment and leaving the hole in an area of flat retina marking the original position of the detachment. Some help in its location may be obtained from the patient's history, for he may indicate the initial position of a loss of field, or the appreciation of a black spot, or flashes of light in a definite direction. The proximity of a focus of old choroiditis or areas of recent hemorrhage is frequently a useful guide; and the use of red-free light is helpful, since a greater contrast is obtained when the free edges of the opaque retina are accentuated against the black choroid." Holes in the extreme periphery may be disclosed by transillumination.

Localization of the tear. In spite of many schemes and plans advanced to localize the tear more accurately and with more scientific precision, the original Gonin method has remained in favor, supplemented by a few simple procedures applied at the time of operation. Many authors, hoping to obtain more precision, have calculated the distance and direction of the tear by angular measures and tables of concordances; some utilized the perimeter and concave mirror (Dor, Dupuy-Detemps et al.), others, the perimeter combined with the direct ophthalmoscope (Guist, Lindner). Weve used an eye of substitution. Stine advocated the perimetric method with conversion tables of his own devising. Because these methods at their best are not infallible and at their worst, time consuming and difficult, they have been largely abandoned. The present and sufficiently accurate method used by many surgeons consists of an estimation of the direction and distance of the tear by Gonin's method, repeated several times. This is done prior to the operation. When the sclera over the area involved is denuded, a more accurate attempt is made by transillumination, using Arruga's speculum, and various forms of transilluminators. That devised by Lancaster is satisfactory. A preliminary diathermy needle puncture or an electrolysis puncture can be made. The white area of the former or the bubbles in the latter in relationship to the hole can be seen with the direct ophthalmoscope, and the hole accurately localized.

The production of adhesive choroiditis. In 1931 Guist and later Lindner used caustic potash applied to the choroid exposed by a series of trephine holes (1.5 mm.) which penetrated the sclera only. Because of the tediousness and difficulty as well as the danger of vitreous hemorrhage due to perforation of a large choroidal vessel, the development of postoperative uveitis and the danger of thrombosis of a vortex vein this operation has been largely abandoned.

The year 1932 saw the introduction of diathermy coagulation for retinal detachment. Larsson reported his method of surface coagulation applied to the entire quadrant above the separation, eliminating the precise localization of the tear, a feature which appealed to many. The positive electrode was a 2 millimeter ball applied to the sclera over the detachment in many places, the contact lasting 3 to 6 seconds producing a parchment-like sclera. The subretinal fluid was then drained by one or two trephine openings.

The year 1932 also saw the advent of Weve's operation which combined surface coagulation with multiple micropunctures. He later abandoned the surface coagulation.

In the same year Coppez suggested the use of a pyrometric electrode devised by him. As related by Krewson, "The circuit used by him consisted of two wires of different metals (copper and constantan) soldered at their ends, and a current was generated which varied in intensity, depending on the difference in temperature of the ends of the wires. One soldered end was kept at 0 degrees centigrade and the other acted as the electrode. The degree of heat obtained in the tissues was read on a calibrated galvanometer. Coppez placed his electrode, a flat disc 2.5 millimeters in diameter, on the sclera a number of times for 20 or 30 seconds until a temperature of 80 degrees centigrade was recorded by the galvanometer. He did not establish drainage until the end of the operation."

Again in the same year Šafář demonstrated his insulated pins or "nails" of iridioplatinum, 1.5 to 2 millimeters long, single or combined into brushes. These were applied as a barrage around the tear and separation by means of a special pair of forceps, and left in place until the entire number was inserted. The advantage of this method was that the subretinal fluid was not allowed to escape until after the operation was completed; thus a soft eyeball was avoided, and a subsequent puncture or trephine was not necessary.

Walker's contribution was a modification of the Šafář nails or brushes replacing these with shorter micropins; and the design of a delicate special high frequency apparatus, which is the one most commonly used at least in the United States. The micropins are inserted about 2 millimeters apart and a current of 25 to 30 milliamperes are used.

From 1932 to the present a constant search was being made by ophthalmic surgeons throughout the world to obtain more satisfactory results with less trauma. Vogt and Imre in 1934 introduced electrolysis, which had already been used by Verhoeff in 1917, and others before him towards the end of the nineteenth century. According to Krewson, Vogt used a galvanic current of 0.5 to 1 milliampere and a long thin steel needle as the cathode or negative pole. The anode consisted of an electrode in the form of a small ball or plate held in contact with the eye. The needle was introduced through the sclera and choroid and withdrawn rapidly. This procedure produces coagulation in the choroid due to the liberation of anions at the anode, as shown by the presence of free hydrogen bubbles. Recent advocates of electrolysis are inclined to use somewhat higher currents. Gradle (1936) uses about 3, and Moore seldom less than 5 milliamperes. It is Walker's first choice of operation.

The three methods therefore used in the modern operation are: (1) diathermy coagulation, (2) electrolysis, (3) surface coagulation. The invention of new instruments and methods of applying them continues apace. Arruga especially has been fertile along these lines, devising tiny threaded plugs to close the trephine openings in cases of perforation of the choroid, lancets for orientation, and a retractor. The last is invaluable. Strampelli's "diathermophanoscope" embodies what is probably a useful idea. It is briefly, a transilluminator and diathermy handle all in one. Meesmann modified Coppez pyrometric electrode, by employing a fine pointed pyrometric electrode in a curved quartz tube with changeable point. Langdon uses the Shahan thermophore at a temperature of 65 degrees centigrade for 1 minute to produce surface coagulation. Gradle and Meyers (1938) and others have devised various electrodes particularly suitable for surgery around the macular area. The LaCarrière electrodiaphake, with which I am sure you are all familiar, has enjoyed a wide and justifiable reputation. The bent and beveled glass tube containing the platinum wire electrode permits the instrument to be applied beneath muscles and behind the globe. The bipolar electrolytic instrument introduced by Von Szily and Machemer in 1936 and described in detail in the *Traite d'Ophthalmologie* by Veil and Dollfus offers many advantages to the use of the usual electrodes. I do not know if they can be obtained in this country.

Each of the three methods of surgical treatment has its ardent advocates. The trend, however, is away from the exclusive use of a single method, and most surgeons are now using a combination of diathermy, electrolysis, and surface coagulation. As time goes on and reports come in, our knowledge will increase and one can readily foresee a standard operation evolved. Both Walker and Peter, for example, use electrolysis to supplement diathermy in the closing of small tears and to reduce to a minimum hemorrhage from retinal vessels. They use it in macular holes and to visualize the correctness of the location of the tear (ophthalmoscopic study). Diathermy puncture is now of two types, the juxtachoroidal and the perforating. The needles are becoming finer and shorter. Juxtachoroidal punctures are

used to isolate the tear by a barrage over the area of separation, the perforating punctures are used to attack the tear itself. The increasing tendency is to operate under the direct control of the ophthalmoscope. A few punctures are made, and then the result noted with the ophthalmoscope, a few more punctures, then observation and so on. It therefore is obvious that drugs which will cloud the cornea should not be employed. Surface coagulation, according to Peter, is indicated to create a sufficient number of points of choroiditic adhesive spots throughout the separated area.

To summarize briefly, the modern trend of the operation is as follows. The tear or hole is localized as accurately as possible and a surface mark placed on the sclera with diathermy. The localization is verified by transillumination either applied to the sclera and observed with the ophthalmoscope, or by shining the light from the ophthalmoscope through the pupil in the direction of the tear and noting a spot of light on the sclera. The hole is further localized by the insertion of an electrolysis needle or perforating diathermy needle and its appearance noted with the ophthalmoscope. The tear is then surrounded by perforating diathermy punctures, except in the macular area. The needles are introduced and left in place until the entire area of the separation has been treated by surface coagulation and electrolysis, or juxtachoroidal diathermy punctures. Some surgeons (Peter) prefer to cover the entire area with negative galvanic needles (½ to ¾ mm.) of perforation, and in addition use catholysis freely in the region of the tears. I am inclined to agree with Weve, however, that it is unnecessary to do more than seal off the tear. Insertion of pins over the entire area of the separation except where there is not a hole found is, to my mind, unnecessary mutilation.

It is perhaps pertinent to mention here another operation which may be found to be useful in cases not suitable for the above operations. I refer to the sclerectomy of Mueller modified by Lindner under the term of "eyeball shortening operation." This operation is described and illustrated by Pischel and Miller who report a successful outcome in what otherwise probably would have been a hopeless case. It consists of an elliptic excision of a piece of sclera over the detached area, great care being taken not to injure the choroid. A case of retinal detachment associated with a scleral ectasia was successfully treated by me. The entire staphyloma was excised, more or less according to Mueller's technique. I am convinced that no other operation would have succeeded in this case.

Anesthesia. Local anesthesia is unsatisfactory. It should be used only when other methods are contra-indicated. Avertin anesthesia is the one of choice, if it can be safely used. Its advantages are: (1) perfect anesthesia, (2) a free field for operating unhindered by the anesthetist, (3) slight danger of postoperative nausea, (4) no disturbance of the conjunctiva and cornea as is caused by local anesthesia, (5) no risk such as is encountered in gas-ether in the presence of a diathermy current. If avertin cannot be used, ether may be fairly safe if a wet towel is so placed as to prevent ether fumes from reaching the field of operation.

Postoperative and convalescent care of the patient. How long one should keep a patient absolutely quiet in bed with eyes blindfolded is a debated question. The "loch brille" or pin-hole glass of Lindner is indispensable to help keep the eye fixed when the bandages are removed. Another method is that of Arruga, who sews the lower lid to the eyeball with a suture through the inferior rectus. There can be no hard and fast rule, since the healing process varies with each case. It is considered wise to keep the patient as quiet as possible in the hospital until the puncture points have started to become pigmented, a condition which varies from 2 to 5 weeks, sometimes longer. It can thus be seen how important is frequent postoperative ophthalmoscopic examinations.

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TUMORS OF THE UPPER JAW

Particularly Tumors Related to the Sinuses

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THE upper jaw is subject to the development of practically all of the tumors that involve bony tissue and in addition may be the site of origin of cystic and calcified tumors of the odontome group. Furthermore, it may be invaded by tumors originating within the accessory nasal sinuses or by tumors of adjacent tissues within the oral cavity or nose.

Malignancies of the upper jaw and sinuses have been studied and reported upon at great length so it will be my purpose to discuss more particularly the diagnosis and treatment of the more common benign tumors and certain unusual tumors involving this region that are of interest to the otorhinolaryngologist.

ODONTOMES

These tumors arise from the cells that are concerned with tooth development and may be conveniently classified as follows[1]:

I. Epithelial odontomes. Tumors in which the abnormal development takes place in the dental epithelium.
   1. *Dental or root cysts.* These develop at the root ends of teeth that have erupted. Pulpal and root end infection, and pulp death of traumatic or chemical origin are apparently the irritative factors in their development. They may occur at the root ends of deciduous teeth. They may also develop in an epitheliated granuloma left in the alveolar process at the time of extraction of an infected tooth.
      A. Indeterminate type dental cysts occur in any portion of the jaw. They are frequent in the region of the angle or ascending ramus and may be multiple. They are not attached to the root of a tooth infected or otherwise, nor will there be a history of the extraction of such a tooth. They also occur in regions where supernumerary teeth are most frequently found and may be due to supernumerary anlagen.
   2. *Dentigerous or follicular cysts.* In these cysts, the wall embraces not a root but the crown of a completely or partially formed unerupted and usually misplaced tooth. Some of these cysts contain cells typical of the adamantinoma.
   3. *Adamantinoma or multilocular cysts.* These tumors show columns or masses of epithelial cells of the enamel organ types—ameloblasts-cuboidal cells, and stellate reticulum. They may be found and operated upon in an early stage when they are not clinically cystic, but rather of a solid consistency. Microscopic examination, however, nearly always shows cell degeneration and beginning cyst formation of the epithelial masses. The term "epithelioma" should *not* be employed in the consideration of these tumors.

II. *Composite odontomes.* Tumors in which the abnormal development takes place primarily in the dental epithelium, and secondarily in the dental papilla, and may occur in the follicle also.
   1. The abnormal development of the dental epithelium is such that the formation of numerous irregular dentine papillae results, and are calcified in one mass or sporadically.
      A. Complex composite odontomes. When tooth structure is shown in the microscopic section and not in the gross specimen which appears like an irregular mass of bone.
      B. Compound composite odontomes. A large number of tooth elements are present. They may be fused or be separate within a cyst cavity.
   2. The abnormal development of the dental epithelium is such that the formation of two or more tooth-like dentine papillae results and are calcified as one mass.
      A. Geminated composite odontomes. Present fusion of teeth combined with malformations, such as masses of dentine and cementum.
      B. Gestant composite odontomes. One tooth develops within another.
      C. Enamel nodules or enamel pearls.
   3. The abnormal development of the dental epithelium is such that the formation of a dilated portion of the dentine papilla results and is calcified as one mass.
      A. Dilated composite odontomes.
         a. Fusiform type: presents a widely dilated or hollowed-out foot with a normal or semiconical crown.
         b. Coronary type: presents dilatations and malformations of the crown portion of the tooth.
         c. Radicular type: presents irregular calcified masses of dentine and cementum projecting from one surface of the root.

III. *Connective tissue odontomes.* The abnormal development takes place in the dental tissues of mesoblastic origin alone. (The dental follicle.)
   1. *Cementomes.* Consist of solid irregular masses of cementum (1) that may develop about the roots or crown of a tooth that eventually erupts, after which the cementum may continue to enlarge; or (2) may surround and destroy an unerupted

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[1]This classification is a modification of the British Dental Association classification.

immature tooth. These masses enlarge and expand the alveolar plates.

2. *Fibrous odontomes.* Apparently the same type of tumor as central fibromas (benign osteogenic tumor), and the fibromas that develop from nerve sheaths. The diagnosis of a fibrous odontome is presumed when the tumor is associated with an unerupted malformed tooth or other dental anomaly.

This classification, based on a very extended study by a committee of the British Dental Association, is to my mind most practical for the surgeon called upon to treat these conditions. Other classifications that have been proposed by pathologists tend to confuse rather than help the surgeon in the diagnosis and treatment of the individual patient. For instance, in many texts, dental root cysts (radicular cysts) are considered to be an inflammatory cyst and not a cystic tumor. While these are from the standpoint of etiology associated with root end infection, traumatic or chemical pulp death or residual alveolar process infection, their clinical course in so far as the destruction of bony tissue and the involvement of the sinuses is concerned, cannot be differentiated from that of the dentigerous cyst. Furthermore, the microscopic examination of cyst walls of both types fails to reveal any diagnostic features that differentiate the cyst wall of the dental root cyst from that of the dentigerous cyst. It is a well known fact that examinations of serial sections of the walls of dentigerous cysts show that some of them are at least potentially adamantinomas. These findings convince me that these cystic tumors should be classified in one group as epithelial odontomes and not considered separately, sometimes even in separate chapters as is the case in some textbooks. Consequently, the dentigerous cysts of the maxilla present potential problems from a tumor standpoint that must be kept in mind in the consideration of the operative techniques designed to prevent the development of persistent fistulas between the mouth and the maxillary sinus or the floor of the nose by leaving in the major portion of the cyst wall.

Cystic odontomes of the dental root and dentigerous types may develop in the anterior, the lateral, or posterior portions of the maxilla. As already noted, their clinical manifestations, growth, and effect upon the bony substance of the upper jaw and encroachment upon the sinuses are quite similar. The rate of enlargement of a cyst varies considerably and is difficult to determine as most patients are operated upon soon after the discovery of the presence of a cyst. Occasionally one can locate a roentgenogram taken some years previously, showing beginning cyst formation that was either not diagnosed or was neglected. In the case of dental root cysts, one may at times estimate the duration of the cyst by the date of a severe dental traumatism, the devitalization of a tooth or the insertion of a synthetic porcelain filling. These cysts may be found at any age, although dentigerous cysts are more common during the period of the development and eruption of the permanent teeth. The direction of the extension of the cyst varies considerably. They may grow more or less equally in all directions or may extend largely in one direction. They tend to project on the labial or buccal surface of upper jaw, presenting as a more or less rounded prominence. This may be soft, hard, or compressible with crepitation, depending upon the amount of loss of the overlying bone due to resorption of the alveolar plate brought about by the presence of the enlarging cyst or the presence of newly formed bone overlying the cyst wall.

These findings may also be present and demonstrable in the hard palate or the cysts may extend upward to elevate the floor of the nose to a considerable degree or may obliterate the entire maxillary sinus and even extend farther without any buccal or palatal evidences of extensive cyst formation. Cysts may expand and thin out the overlying tissues to rupture or they may be excised on suspicion of an abscess formation following which there may ensue a very low grade secondary infection. The cyst contents vary markedly in consistency and color—depending upon the types of degenerative processes affecting the epithelial and connective tissue of the cyst walls together with the character of the exudates or presence of hemorrhage, modified at times by low grade infection. Very rarely, an extremely acute infection may for no apparent reason involve a cyst that has been developing for months or years without producing any symptoms. Discharging sinuses and infections of a cyst in the maxillary sinus region are often confusing in the matter of correct diagnosis and treatment.

Diagnosis. Careful clinical examination of the oral region together with rhinoscopic examination may establish a presumptive diagnosis of the presence of a cystic odontome. If permanent teeth are missing with no history of their extraction, the presence of a dentigerous cyst should be suspected. Roentgenographic examination is essential to determine the position and extent of the tumor, the presence of unerupted teeth, etc.

Regular intra-oral dental films are useful but occlusal films of larger No. 2 size, 2¼ by 3 inches, taken in the anterior and the oblique lateral pro-

jections are of greater service. A postero-anterior sinus film, Waters-Waldron projection, and direct or oblique lateral films of the maxilla are helpful in predetermining the method of treatment.

Treatment. Cystic odontomes if small may be completely removed by the enucleation of the cyst walls from the surrounding bone and the incision then closed by suturing. In the event that the cavity is not obliterated by the organization of the blood clot it becomes necessary to dress the cavity with a lubricated antiseptic gauze dressing or use an obturator until the cavity granulates and fills in to a level approaching the surface of the jaw. This is the method of choice in larger cysts that do not expose the mucous membrane lining of the nose or that of the maxillary sinus. If the membranes are exposed, complete enucleation usually results in extensive perforations into the nose or maxillary sinus that produce permanent fistulas with accompanying discomfort and annoyances that are not corrected or eliminated by dental restorations. To obviate such unfortunate sequels, the Partsch operation has been employed with considerable success. In this procedure, a large window is made on the buccal aspect of the cyst by the excision of a section of its wall, and the deeper portions of the wall are left undisturbed to protect the nasal cavity or the maxillary sinus. The margins of the window in the cyst wall are sutured to the margins of the incision of the mucous membrane.

The postoperative treatment consists of using gauze dressings or employing an obturator until the cavity has filled in to a level that approaches the surface. This operation is based on the fact that cystic odontomes stop growing when they are kept open and tend to become obliterated by a filling-in process the exact nature of which is not well understood. The probable explanation is that the connective tissue of the cyst wall proliferates with subsequent degeneration of the epithelial lining that was left in at the time of operation. The filling-in process is considerably slower after Partsch operations than when a complete enucleation of the cyst walls has been performed, in which the underlying bony cavity is intact and produces granulations from the entire cystic area.

In order to determine whether a complete enucleation of the wall or a Partsch operation should be performed, I make it a routine first to establish an adequate window on the buccal surface to expose the cyst cavity. The cyst contents are then completely removed by gauze wiping or, if necessary, by irrigation. The cyst lining is then carefully examined for evidences of perforation into the floor of the nose, the maxillary sinus, or through the palatal process. This may be ascertained by probing carefully with a blunt instrument. If all surfaces are found firm and resistant to the pressure of the probing, the complete removal of the cyst wall by dissecting it from its bony cavity is, in my opinion, the method of choice.

If the probing demonstrates but very small perforations of the walls, careful sharp dissection will separate the cyst wall from the mucous membrane without danger of actual perforation and the formation of a fistula. Larger areas of exposed nasal or sinus mucous membrane should be protected by leaving in the cyst wall by the Partsch procedure.

Cysts that encroach upon the maxillary sinus present operative problems that warrant careful pre-operative study. In those cysts that are entirely situated posteriorly without an extension of the cyst beneath the floor of the nose, decision must be made whether or not the cyst cavity should be made to communicate with the remaining portion of the maxillary sinus by removal of the entire intervening cyst wall, followed by the establishment of an adequate intranasal window in the inferior meatus of the nose. This is, in effect, the Caldwell-Luc, so called radical antrum procedure, in which the oral incision is closed at the end of the operation. This method, in my experience, has been uniformly satisfactory in every way and has greatly shortened the postoperative treatment. In most instances only a few treatments with applications through the intranasal window are necessary to secure a healed dry antrum and cyst cavity. This obviates weeks or months of intra-oral dressings with their accompanying annoyances or the use of an obturator for a long period after performing the Partsch operation. Formerly, I always removed the cyst lining from the lower portion of the cystic area in addition to removing the upper portion of the cyst wall that extends into the maxillary sinus.

This leaves the denuded bone of the cyst cavity in approximately the same condition as in the Caldwell-Luc procedure for chronic maxillary sinusitis after the removal of the infected membrane. The postoperative healing apparently follows the same course to complete resolution. The growth of a cyst, however, may encroach upon the root ends of underlying teeth, producing resorption of the apical portion of the roots without cutting off the blood supply of the dental pulps as there develops an anastomosis of the vessels of the cyst wall with those of the pulp. On this account, useful vital teeth may be retained

to function normally for many years, provided the root ends are not exposed by the surgical removal of the cyst membrane. Pre-operative dental x-ray films will usually show the intimate relationship of the cyst wall to the underlying root ends and will determine the necessity of leaving the cyst wall to protect the vitality of the teeth. In more recent cases, I have left this lower portion of the cyst wall undisturbed with uniformly good results in so far as the healing of the maxillary sinus cystic cavity is concerned.

Another problem that warrants detailed discussion is that of the treatment of large cysts that not only obliterate the maxillary sinus, but also extend under the floor of the nose sometimes past the midline beneath the floor of the nose on the opposite side. If a Partsch operation is performed, the postoperative course may extend over months or a year or more. If a Caldwell-Luc cyst procedure is undertaken, the cystic area beneath the floor of the nose constitutes a pocket where exudates may collect, become foul smelling, and give the patient no end of annoyance and discomfort. To prevent this postoperative condition, a two stage procedure has been undertaken with gratifying results. The first procedure is a Partsch operation exposing the anterior extension of the cyst cavity but not uncovering it completely on its labial aspect. It is then treated after operation in a routine manner by gauze packing two or three times a week until the anterior extension of the cyst has filled in sufficiently to obliterate that portion of the cavity that was present beneath the floor of the nose. This may take 3 or 4 months to accomplish, after which, the Caldwell-Luc cyst procedure may be undertaken and the oral incision that had remained open since the first operation is closed by undermining and suturing. The comfortable and satisfactory end-results have fully justified the time and care spent on several cases that have been treated in two stages in this manner. The prolonged period of dressings and the greater or lesser deformities that have been avoided amply repay the patient for the confidence and co-operation shown in accepting two operative procedures in order to obtain a more satisfactory ultimate result.

In case a portion of dentigerous cyst wall is left in position to prevent fistula formation or to shorten the postoperative course as already outlined, it is essential to have a microscopic examination made of that part of the cyst wall removed with the window. Any thickened or projecting portion of the cyst wall should also be excised and examined to be sure that the epithelial cells are not of the adamantinoma type. Such a condition is found very rarely but must be kept in mind, and, if present, excision of the entire cyst wall or cauterization by diathermy should be employed.

Should permanent fistulas develop to communicate with the nose or maxillary sinus, carefully made dental restorations will largely overcome the discomfort incident to such perforations.

Atypical cystic tumors of the maxilla that involve the maxillary sinuses have come under our observation several times. They have presented combinations of cystic areas and masses of fibrous tissue and bone in association with unerupted malformed teeth. The exact diagnosis may be somewhat obscure but is likely to be a variant of a composite or fibrous odontome or an atypical osteitis fibrosa cystica—but microscopic examination will establish the benign character of the tumor tissue. The treatment is in general accordance with that already outlined for cystic odontomes depending largely upon the position and extent of the tumor.

The adamantinoma of the maxilla is very slow growing with insidious onset and consequently presents considerable difficulty in the matter of early diagnosis. Symptoms may be practically absent or there may be merely an indefinite feeling of pressure or tension. Slight neuralgic pains or tenderness referred to the maxillary sinus area may be noticed by the patient. In other cases, the symptoms are localized to the teeth and alveolar process and are likewise ill defined. This tumor may be present for many years before any definite enlargement of the maxilla may be demonstrated. Dental roentgenograms tend to be inconclusive and routine sinus films may show but slight or moderate clouding of the maxillary sinus.

These considerations account for the difficulties in diagnosis and the delay in instituting adequate treatment for this tumor. Months and years of valuable time may be lost while the patient is undergoing dental treatment or repeated punctures and irrigations of the maxillary sinus. Intranasal window operations may be performed to improve sinus drainage without the removal of tumor tissue for biopsy and thus more time may be lost. I have seen several patients whose histories suggested the presence of an adamantinoma for many years before the diagnosis was established.

I hesitate to bring into this discussion such a controversial subject as the relative merits of the intranasal antrum operations versus the canine fossa approach to the sinus used in the Caldwell-Luc procedure in the treatment of chronic maxillary sinusitis, realizing that men who employ

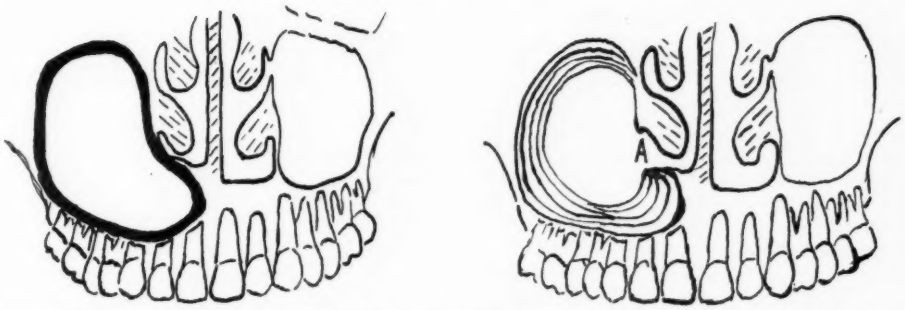

Fig. 1. Two stage operative procedures for cystic tumors that obliterate the maxillary sinus and extend beneath the floor of the nose. Stage I: Partsch operation by means of a buccal window through which the cyst cavity is dressed. Stage II: 3 to 6 months later as soon as the cavity beneath the floor of the nose has become obliterated. *A*, Intranasal window established and surgical closure of the operative approach used in Stage I.

the Caldwell-Luc procedure are greatly in the minority. While I concede that in the hands of skilled rhinologists the intranasal procedures are effective and satisfactory in every particular, I do feel that the buccal approach to the maxillary sinus gives better access to, and more complete visualization of, the operative field, thus affording more thorough and accurate surgical treatment of the condition present.

In my experience there have been no disadvantages associated with the Caldwell-Luc procedure other than swelling of the cheek that lasts but a few days. I am sure that rhinologists who employ the Caldwell-Luc procedure will quickly develop a diagnostic sense that will differentiate between the varied appearances of chronic inflammation of the sinus mucosa on the one hand and the more serious tumors and the malignant tumors on the other hand.

For this reason, I would urge that rhinologists employ the Caldwell-Luc procedure much more frequently especially in cases with obscure symptoms in order to make possible the earlier diagnosis of tumors of the sinus and to avoid the humiliation incident to prolonged sinus treatments in tumor cases.

The nature of the tumor cannot be diagnosed by visual examination alone and biopsy is necessary to determine the treatment to be instituted.

Adamantinomas of the maxilla and sinuses must be considered as serious tumors that may endanger the life of the patient on account of inoperable extensions or the onset of meningitis due to the extensions of the growth and secondary infection. The prognosis varies with the position and extent of the tumor and the greater or lesser degree of histological activity of the tumor cells. The more or less favorable position of the tumor is a large factor in its curability, and it is obvious that the inferior anterior location affords a much more favorable prognosis than does a location extending posteriorly and superiorly. This corresponds with the conclusions of Öhngren who divides tumors of the upper jaw and antrum into two groups by a plane which passes from the inner canthus in a direction backward and downward to the angles of the mandible. It must be remembered that an unsatisfactorily prepared and stained frozen section may present difficulties in diagnosing adamantinomas from adenocarcinoma and at times it may be wise to postpone the destruction of the tumor by cauterization or with surgical diathermy until the day following the biopsy. This will permit the preparation of a well stained permanent section making accurate diagnosis and the determination of the degree of cell activity less difficult.

Adamantinomas must be completely removed and destroyed in order to prevent recurrence. Surgical diathermy is the method of choice and should be employed in a thorough and painstaking manner. The bony wall surrounding the tumor tissue should be cauterized thoroughly in every portion of its surfaces and any regions in which the tumor may have extended through the antral walls to the soft tissues should be carefully treated with a protected endotherm point. The same meticulous care should be employed in destroying the tumor tissue that may have extended into the ethmoidal sinuses. These tumors are resistant to radiation, although radium may be employed with apparent success in regions that are inaccessible to adequate treatment by diathermy. Extensions of adamantinomas beneath the orbit may produce orbital displacements, exophthalmos, and a variety of inflammatory conditions of the

orbit and globe. It may be occasionally necessary to remove the eye but usually the displacement or inflammatory reaction subsides as soon as healing is complete. The postoperative course may be stormy and painful until sequestra have become separated and are removed, particularly when orbital signs and symptoms were present before the operation. Usually from 6 weeks to 2 months or more elapse before it may be determined that the margins of the necrotic bone may be pried loose and the sequestra can be removed. Healing thereafter is usually without incident and the region becomes comfortable. Examination should be made from time to time in order to be sure that all parts of the original tumor area are well healed and firmly epithelized.

Recurrences of this tumor are due to failure to remove and destroy all tumor tissue. Such recurrences are usually of very slow growth and prognosis is still usually favorable except when situated in the posterior superior regions. It is not wise to attempt a plastic closure of the buccal opening into the operative area for 2 or 3 years, until one is satisfied that there are no evidences of recurrences—an obturator may be made; or the patient may use cotton or gauze to plug the opening at meal times.

Composite (calcified) odontomes may involve the maxilla. These are sometimes associated with areas showing fibrous or cyst formations. Diagnosis is usually not difficult, as roentgenograms usually reveal the nature of the tumor. These tumors are essentially benign and do not endanger life. They do, however, show a tendency to develop acute infections in the tissues adjacent to the surface of the tumor, to produce a cellulitis with abscess formation. Occasionally this may occur without any previous knowledge of the presence of a calcified tumor. Several weeks should elapse following such an infection before any attempt is made to remove the tumor.

The treatment is surgical excision of the entire tumor mass and the operative approach is much the same as for the cystic odontomes. Excision of the calcified tumor may be difficult, requiring painstaking removal of overlying and adjacent bone by means of chisels or burrs in order to make possible the delivery of the tumor from its bed. The resulting defect may present quite a problem on account of an extensive exposure of the sinuses and nose together with loss of the alveolar process ridge. The operative approach is from the buccal or the incision may be made along the alveolar process ridge. Mucoperiosteal flaps may be retracted palatally and buccally to provide a wide exposure of the tumor area and may at the conclusion of the operation be sutured to close off the operative field from the mouth if conditions permit. These tumors are not likely to extend beneath the floor of the nose and the sinus tumor cavity may be made to communicate with the nose by means of a naso-antral window to thus shorten the postoperative course as outlined in the discussion of the treatment of cystic odontomes.

Fibrous odontomes or central fibromas of the maxilla can rarely be diagnosed before operation, as the x-ray appearances are similar to those of the cystic odontomes. Fibromas are rare and biopsy is necessary in order to complete the diagnosis. The treatment is complete excision and the operative and postoperative treatment corresponds with that of the cystic odontomes in which the entire cyst wall is removed.

Cementomas develop slowly but may attain a considerable size to encroach upon the maxillary sinus. The x-ray appearance of these tumors is similar to the composite odontomes and the operative and postoperative treatment is essentially similar in every respect.

As already noted in the introduction to this discussion, the upper jaw may be the site of any of the tumors that involve bone. These may be classified according to the various modifications of the Codman registry nomenclature of the American College of Surgeons.

I. Metastatic tumors of the jaws are rare. Metastases of carcinoma from the breast, thyroid, prostate, ovary, etc. are on record. Sarcoma and hypernephroma metastasizing to the jaws have been reported.

II. Periosteal fibrosarcoma is a less malignant form of sarcoma that has been found lying next to the bone of the jaws. It arises in the outer layers of the periosteum or in the adjacent fascia or tendinous insertions. It does not invade the bone but may cause pressure absorption. It does not form osteoid tissue, cartilage, or bone. Metastasis infrequently occurs.

III. Osteogenic tumors are derived from cells concerned in the development of bone and cartilage, etc.

A. Benign osteogenic tumors:

1. Hyperostoses are inflammatory enlargements of a diffuse type that frequently involve the molar region and tuberosity of the maxilla. Leontiasis ossium is of this type.
2. Exostoses may occur on the lingual surface of the mandible and in the center of the hard palate, torus palatinus. They have been noted to occur frequently in the tuberculous.
3. Osteomas may develop in any portion of the mandible or maxilla. When developing in the region of the condyle, the ascending ramus is lengthened, causing opening of the bite. In the upper jaw, the maxillary sinus, nose, or orbit may be involved. The other facial bones may develop these tumors.

4. Fibromas may occur as central tumors or in the deeper layers of the periosteum.
5. Chondromas may develop centrally or from the alveolar margins, the palate, the coronoid, or the condylar cartilage. Pure chondromas of the jaw are rare. Tumors of this group may show combinations of cartilage, fibrous tissue and bone.

B. Malignant osteogenic tumors: Osteogenic sarcomas may arise in the central portions of the jaw and in the deeper layers of the periosteum or may arise alone from the subperiosteal layer. It is often difficult to determine the exact site or origin, particularly in the maxilla where such tumors may start in the subperiosteal layer of the maxillary sinus membrane. Types:
1. Those destroying bone—osteolytic.
2. Those forming bone—sclerosing.
3. Those forming cartilage—chondrosarcoma.

IV. Inflammatory conditions that may simulate tumors of the mandible and maxilla.

A. Osteoperiostitis (osteomyelitis) occurring in atypical forms may occasionally simulate a primary tumor of the mandible or maxilla.
1. Traumatic periostitis may occur in chronic form without an acute onset. Hemorrhage and resulting repair, cartilage, and bone formation may closely simulate tumor formation. A few months' observation will clear up the diagnosis.
2. Syphilitic periostitis or osteoperiostitis occurring in the second or third stages of lues may resemble a sarcoma.
3. Infectious osteoperiostitis—osteomyelitis.
   a. Pyogenic infection of a low grade type may produce tumefaction that necessitates observation over a period of time in order to rule out tumor formation.
   b. Tuberculous periostitis and osteitis may for a considerable time simulate tumor formation.

B. Actinomycosis of the tissues surrounding the mandible, particularly when hard, may for a time simulate sarcomas. The bony substance of the jaw is rarely if ever involved and the contour of the mandible will be seen to be normal in the roentgenogram.

C. Osteitis fibrosa cystica occurs frequently in the mandible and maxilla. It is characterized by cystic areas without an epithelial lining, fibrosis, condensing osteitis. Other bones may also be involved. This condition may be associated with parathyroid tumors and disturbances in the calcium-phosphorus balance.

V. Central giant cell tumors are identical in structure to the giant cell epulides. They develop centrally and expand the jaw until the cortex is reduced to a thin shell or becomes destroyed. They are usually soft and red and present a varying number of multinucleated giant cells in a loosely woven connective tissue stroma.

VI. Angiomas, benign or malignant, of the bony substance of the jaws are very rare, but have been recorded.

VII. Ewing's sarcoma, endothelioma, may develop in the mandible in several areas simultaneously, destroying the bone. The tumor consists of small, polyhedral cells with no intercellular substance. Fever, pain, and the x-ray appearance may simulate osteoperiostitis—osteomyelitis.

VIII. Myelomas may involve the mandible and skull along with other bones. The myelitic substance of the bone is destroyed by the tumor cells. Albumosuria is present.

Metastatic tumors of the maxilla are rare and usually insidious in their course, presenting difficulties in diagnosis except by biopsy. The prognosis depends upon the type of tumor, its degree of malignancy and the prognosis of the primary tumor. Many of course are inoperable on this account. Metastases to the jaws of carcinoma of the breast, thyroid, prostate, and ovary have been reported as well as sarcomas and hypernephromas. A benign tumor of the thyroid metastasizing to the mandible has been reported by Ivy.

Periosteal fibrosarcoma arising on the external surface of the maxilla may necessitate the exposure of the maxillary sinus in its removal by excision.

Osteogenic tumors of the maxilla may be benign or extremely malignant osteogenic sarcomas. The benign tumors are the hyperostoses, exostoses, osteomas, chondromas, and fibromas.

Hyperostosis may produce a massive enlargement of the molar region and tuberosity. The buccal and palatal aspects are more particularly involved although the tumor may extend upward to encroach upon the maxillary sinus. Removal of the excess bone by chisels and curets to restore a normal contour gives satisfactory results in that production of new bone ceases. Should the maxillary sinus be exposed in the surgical procedure, it usually does not require any special treatment as the mucoperiosteal incisions may be sutured.

Central osteomas, fibromas, and chondromas may also encroach upon the maxillary sinus, and their surgical removal may produce large openings into the sinus cavity. These may usually be closed by suturing. Occasionally it may be wise to make an antronasal window through which postoperative treatment may be carried out.

Osteogenic sarcomas of the maxilla are relatively infrequent—about 10 per cent of the primary and secondary malignant tumors involving the maxillary sinus will, on microscopic examination, be found to be osteogenic sarcomas presenting wide variations of sarcomatous cellular detail which accounts for the fact that these tumors have been designated as spindle cell sarcoma, round cell, myxosarcoma, osteosarcoma, chondrosarcoma, mixed, angiosarcoma, or combinations of several types. These tumors may arise in the deeper layers of the periosteum or beneath the periosteum in the cortical or medullary portions of the alveolar process or body of the maxilla. In these cases the early symptoms may be merely

obscure dental pain or loosening of teeth, which progresses to an apparent tooth or jaw infection with suppuration and necrosis. On the other hand, the tumors may arise from the periosteum of the maxillary sinus and may grow to fill the antrum before producing definite symptoms of tumor formation. Local ulceration of the tumor within the sinus may lead to symptoms of nasal and sinus infection; such as obstruction or discharge of a purulent or blood stained nature. Later nasal polyps may be seen on examination and bleeding from the nose may become frequent. The condition may be erroneously diagnosed as a chronic infection of the maxillary sinus and much valuable time is thereby lost. Continuing to grow, the tumor may perforate the bony walls and extend into the cheek, the orbit, the nose, or the palate.

Enlargement of the cheek of recent origin in a middle aged person is usually malignant if not of inflammatory dental origin and should not be neglected. At times, displacement of the eye may be noticed a few weeks after the onset of nasal symptoms. Early diagnosis is most essential in order to make possible adequate treatment of this extremely malignant tumor. Persistent facial pain aggravated by lying down, increasing nasal obstruction of short duration, lacrimal duct obstruction, mucoid or suppurative nasal discharge, particularly if blood stained, are symptoms that should be considered due to a malignant tumor until the condition has been proved to be inflammatory or benign. Roentgenograms should be made, using the standard and special projections to show the maxilla and the sinuses. Careful examinations of the films should be made to determine the presence of defects of the bony walls, which almost invariably indicate destruction by tumor formation. I have seen but one patient in which such a defect proved to be due solely to chronic inflammation.

These symptoms and examination findings should convince the surgeon that the condition is a malignant tumor and he should plan the treatment accordingly. At operation, a frozen section should be made to determine the diagnosis and the degree of malignancy.

The treatment of osteogenic sarcomas of the maxilla is destruction by diathermy supplemented by radiation therapy; preferably by means of radium emanation or element from within the tumor and sinus area (5). An interval of time between the biopsy and the destruction of the tumor tends to increase the operative difficulties and should be avoided. Intratracheal nitrous oxide is the anesthetic of choice and the operative approach is either through the mouth or by means of a lateral rhinotomy, depending upon the position of the tumor. Primary and secondary bleeding is controlled by packing; if persistent, the ligation of the external carotid artery may become necessary.

This discussion of osteogenic tumors of the maxilla holds true for squamous cell epitheliomas and adenocarcinomas which are much more frequent—about 70 per cent of all primary and secondary malignant tumors of the antrum.

The postoperative course is much the same as has been described in the case of adamantinomas of the maxilla and antrum. Any defects and loss of tissue of the maxilla or cheek may be reasonably well restored by plastic surgery. This should not be undertaken for several years, until danger of tumor recurrence is apparently well past. Dental restorations of the obturator denture type may be necessary to close off the antrum or nose from the oral cavity.

As to chondrosarcoma of the maxilla, Phemister is of the opinion that the term osteogenic sarcoma is used too broadly at present and is of the opinion the malignant cartilaginous tumors may be recognized as a class by themselves and so designated. He reports a case of chondrosarcoma of the maxilla that terminated fatally after two recurrences with metastasis. The microscopic examination showed hyaline cartilage with extremely little calcification or ossification. This tumor filled the antrum to bulge above the gum margin. The recurrences extended through to the nasopharynx, orbit, and the nose.

Osteitis fibrosa cystica is a borderline inflammatory tumor that may involve the maxilla to produce a slowly progressing enlargement of the upper jaw. The overlying soft tissues and the periosteum are apparently not involved by the growing tumor. The molar region and the tuberosity are common sites for the development of this condition and consequently the maxillary sinus may be more or less obliterated by the gradual extension of the process in the upward direction. Symptoms are usually obscure—often limited to a feeling of pressure, slight pain, or recurring neuritis. Later the patient is conscious of an enlargement of the jaw or cheek. These growths may be associated with similar lesions in the long bones and parathyroid tumor or with disturbances in the calcium phosphorus balance. Occurring in the region of the antrum these tumors are of considerable interest to the rhinologist. Some of these growths present multiple cysts readily recognized in the roentgenogram, whereas others show but a massive enlargement of finely trabecu-

lated bone similar to hyperostosis. Treatment is not standardized for this condition. Careful examination should be made to rule out parathyroid tumor. Surgical treatment is usually limited to the removal of enough tumor tissue to correct the enlargement and deformity. These growths tend to be self-limiting and regressive and the postoperative course is usually without incident. Adequate mineral and vitamin therapy is a useful adjunct to surgical treatment in the management of these tumors.

Giant cell tumors of the maxilla occur in two forms: (1) the giant cell epulis, and (2) the central giant cell tumor. The epulis develops in the region of the gum margin but may extend deeply into the body of the maxilla. The central giant cell tumor tends to grow in all directions to involve the maxillary sinus and also protrude on the buccal and palatal aspects of the upper jaw. These tumors may be indolent and slow growing with relatively feeble invasive and destructive qualities or an active malicious growth which increases rapidly in size to destroy the overlying bone and extend into the adjacent soft tissues. The microscopic examination shows large numbers of giant cells in a stroma of actively growing cells of both round and spindle type. Giant cell tumors have been studied extensively with reference to their etiology, pathology, and the relationship of these tumors to solitary bone cysts and osteitis fibrosa cystica. Some authorities favor radiation therapy rather than surgical removal by curettage and cauterization. Others stress the fact that many of these tumors are not radiosensitive and when so treated valuable time is lost and subsequent surgical treatment is of necessity more radical and mutilating. Surgical treatment is the method of choice in giant cell tumors of the maxilla. Removal of the tumor tissue by enucleation and curettage of the bony cavity followed by cauterization is effective in eradicating this tumor. The operative defect will determine the nature of the postoperative treatment and the handling of the problem of sinus exposures in a similar manner to what has already been discussed.

Squamous cell epitheliomas are by far the most common primary and secondary malignant tumors of the maxillary sinus. Adenocarcinoma occurs about as frequently as the various sarcomas that may be grouped as osteogenic tumors. The symptoms are about the same as those noted in cases of adamantinoma and osteogenic sarcomas and the treatment is essentially electrosurgical and by radiation therapy rather than by the radical surgical procedures in vogue two decades ago.

The degree of malignancy as shown in the microscopic section will determine the technique of treatment. Tumors of lesser malignancy require careful and painstaking destruction of the entire tumor by surgical diathermy and when bone is involved the periosteum is likewise treated to prevent recurrence. Great care must be taken to avoid leaving any tumor tissue in any region, and frozen sections may be made of any suspicious areas. Further destruction by diathermy may be instituted and radium seeds inserted.

Highly malignant tumors should be explored and thoroughly coagulated centrally to provide adequate drainage and to produce a cavity large enough to permit the insertion of radium element and radium emanations may be implanted around the periphery of the growth.

The postoperative considerations and course have already been discussed under adamantinomas and osteogenic tumors.

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NEUROSURGICAL ASPECTS OF FACIAL INJURY

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GROSS injury of the nerve supply of the face is comparatively rare in trauma of this region. This is the more surprising when we recall the rich and complicated nerve supply of the head. Nearly all of the twelve cranial nerves are distributed in this region, including the nerves of special sense—smell, sight, taste, and hearing. Tactile sensibility is transmitted through the fifth cranial nerve by three great branches leaving the base of the skull through three separate foramina of exit. The facial muscles are innervated by the seventh cranial nerve that leaves the cranial cavity through a tortuous bony canal in the petrous portion of the temporal bone.

That this rich nerve supply should escape injury is explained by certain embryological and anatomical factors. The base of the skull, it will be remembered, is embedded in cartilage, and becomes ossified comparatively early in life. The base of the skull becomes a massive block of cancellous bone whose otherwise cumbersome weight and size are relieved by numerous cavities lined by mucous membrane and connected with the nose, the paranasal sinuses.

Trauma severe enough to fracture this basilar block of bone produces only fissures unless it is of such severity that the skull is crushed when death immediately ensues. Though fissure fracture of the base of the skull may cause grave consequences from resulting intracranial hemorrhage, it is only when the fracturing fissure passes through, or in the neighborhood of, one of the many foramina of exit of the cranial nerves that injury to these structures takes place.

As there is little or no displacement of bone fragments in fractures of the base of the skull, the fractures themselves are disregarded and our attention is centered on the complications—hemorrhage, edema, or nerve injury.

The characteristic reparative process of the bones of the skull is of great surgical importance. The massive temporary callus following fractures elsewhere in the body is not seen. Permanent repair of fracture of the skull is also accompanied by a minimum of permanent callus. Thus no bony masses mark the site of repair and the line of fracture returns almost to its normal configuration.

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This fortuitous phenomenon prevents these fractures from either encroaching on the cavity of the skull proper, or on the foramina of exit of the cranial nerves. If compression of a nerve occurs from hemorrhage immediately following injury, we may expect the compression to subside promptly with absorption of the clot. We also expect no permanent interference in the function of the nerve from resulting callus formation or exostosis.

Therefore, the dysfunction of the cranial nerves following trauma of the head is usually transient paralysis. Unless the particular nerve is actually severed or crushed by the injury its function returns in a comparatively short time.

Certain nerves seem to be more easily hurt than others. This is probably best explained by the narrowness of their foramina of exit, which permits minimal displacement or hemorrhage to disturb the delicate axis cylinders without gross injury of the nerve trunks themselves. The sixth cranial nerve supplying the external rectus muscle of the eyes is the most commonly hurt. Hence, a transient extra-ocular palsy with diplopia is not uncommon in cases of fracture of the base of the skull. Injury of the other cranial nerves supplying the eyeball and its extra-ocular musculature is much more rare.

In third nerve injury the greatest permanent disability is ptosis of the eyelid because of the deformity produced. Anchoring the lagging eyelid to the frontalis muscle by a fascial band is the best treatment for this defect. The eyelid is elevated to a more normal position and can be raised by contraction of the ipsolateral frontalis muscle.

The next most commonly affected cranial nerve to be injured in fracture of the base of the skull is the seventh, or facial, nerve. Since it supplies all of the muscles of the face, its injury produces marked disfigurement and disability.

A total paralysis of the facial nerve produces complete relaxation of the corresponding side of the face. The patient is unable to close the eye, with resulting danger to that organ. Because the mouth cannot be closed on the affected side, there is constant dribbling of saliva and marked interference with mastication. Even a partial facial palsy is disfiguring. As expressional movements are principally affected, the sufferer feels the embarrassment acutely and begs for relief.

Fig. 1. Fig. 2. Fig. 3. Fig. 4.

Fig. 1. Case 2. Complete dehiscence of the left seventh nerve repaired by 15 millimeter graft from the anterior cutaneous femoral nerve. Before operation. Face in repose.

Fig. 2. Case 2. Before operation. Patient smiling.
Fig. 3. Case 2. After operation. Face in repose.
Fig. 4. Case 2. After operation. Patient smiling and closing the eye.

Fortunately, surgery has something to offer these patients. The deformity of the face may be improved by the insertion of fascial bands in the subcutaneous tissues. These are attached to the angle of the mouth, the nasolabial fold, and to the upper and lower eyelids, and are anchored in the temporal fascia. Such an operation restores the facial symmetry and prevents overstretching of the affected muscles. It is a great relief to these unfortunates, but, of course, does not restore the function to the paralyzed muscles.

Re-innervation of the affected musculature may be accomplished by direct repair of the divided nerve, or by anastomosing a neighboring motor nerve with the distal portion of the paralyzed nerve. The latter operation has enjoyed a good deal of popularity since it was first done by Sir Charles Ballance in 1895.

He divided the spinal accessory nerve in the apex of the posterior triangle of the neck and anastomosed its proximal segment to the distal segment of the freshly divided facial nerve. Later Ballance suggested the use of the hypoglossal nerve. This operation, I believe, is now the more popular procedure since the accompanying movements of the tongue are less disfiguring and disabling than the movements of the shoulder that accompany spinal accessory facial anastomosis.

The results of these procedures, as satisfactory as they sometimes are, do not compare with the results accomplished by direct nerve suture or even to nerve graft of the seventh nerve itself.

Ballance and Duel carried out exhaustive researches on monkeys and showed that grafting the facial nerve in the fallopian canal is usually more successful than grafting of other peripheral nerves.

Unfortunately, too many facial palsies are seen following mastoid operations in which not only may the nerve be severed but there may be actual destruction of a portion of the nerve so that direct suture is impossible. In these cases the insertion of a graft from a superficial cutaneous nerve has brought about results just as satisfactory as the nerve anastomoses and without the accompanying movements of the shoulder or tongue.

Permanent injury to the fifth cranial nerve is seldom seen in facial trauma. When it does occur the only result is anesthesia of the area of distribution of the affected branch, or perhaps paralysis of the muscles of mastication on one side. This leads to little or no difficulty and surgical repair is not indicated.

It is thus seen that practically the only neurological complications of injuries about the face are a transient ophthalmoplegia, anesthesia of the face, or facial paralysis. In rare cases in which permanent nerve injury occurs the only one demanding treatment is paralysis of the seventh or facial nerve.

The operation of choice for facial paralysis is direct suture of the divided nerve. If this is impossible, nerve grafting should be resorted to, and as a last resort, if the previous operations cannot be accomplished, or if the results are not satisfactory, anastomosis of a neighboring motor nerve to the distal portion of the paralyzed nerve may be done.

I have had the opportunity to take part in the treatment of facial paralysis following mastoidectomy. An otolaryngological confrere, Dr. William H. Jenkins, of Washington, D. C., and I have operated on several of these patients with very satisfactory results. The injuries, of course, all occurred to that portion of the nerve in the fallopian canal. They ranged from incomplete division to total division, or to dehiscence of as much as 20 millimeters.

Direct suture was possible in 1 case. Grafting of a portion of the external cutaneous nerve of the thigh, or of the sural nerve from the calf of the leg had to be done in 3 cases. They all showed beginning return of motion in about 5 months. Excellent results occurred in an average of 10 months. In no case was there failure to obtain voluntary motion and complete restoration of the facial symmetry.

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BODY SECTION ROENTGENOGRAPHY AS A DIAGNOSTIC AID TO THE OTOLARYNGOLOGIST

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MANY surgeons are familiar with some form of body section roentgenography and what it can accomplish, but, for the benefit of those who have had no contact with this method, a brief review of its history and the principles involved is in order.

The ordinary roentgenogram is really a composite of all the structures lying in the path of the x-ray beam, because all structures capable of absorbing the ray cast their shadows. Unwanted shadows cannot be separated in ordinary roentgenography except by varying the tube-object relationship and by making stereoscopic films. These leave much to be desired. The superfluous images greatly limit the usefulness of roentgenography, and their elimination has always been one of the chief problems of the radiologist.

Bocage (3) of Paris was the first worker to attack this problem successfully. He found that unwanted shadows could be dispersed to a remarkable degree by imparting a co-ordinated, synchronized movement of x-ray tube and film about a fixed point during the exposure. All objects in the plane about which movement took place would be, so to speak, "in focus" and clearly defined on the roentgenogram, and those outside of the plane, "out of focus" and blurred on the roentgenogram. Bocage devised an apparatus for carrying out this principle and applied for a patent in 1921. He did not construct his machine, which he called the biotome, until 1938 (4), and in the meantime several other investigators working independently had discovered this principle and devised other types of apparatus. Between 1921 and 1938 there appeared the stratigraph of Vallebona, the planigraph of Ziedses des Plantes, the tomograph of Grossmann and Chaoul, the laminagraph of Kieffer, and several modifications of these. Each worker coined a term for the type of roentgenography done with his apparatus, and as a result, the literature contains discussions of "stratigraphy," "planigraphy," "tomography," and "laminagraphy," all more or less synonymous and used indiscriminately. To avoid the confusion which naturally results from such a multiplicity of names, we have strongly urged that "stratigraphy," "planigraphy," etc., be restricted to work done with the apparatus from which each word is derived, and that a generic term be used to cover work done with all these types of apparatus, and have used "body section roentgenography" consistently for this purpose. Among the words suggested by others is Bocage's "radiotomie," which, if Anglicized and popularized, would be most satisfactory because of its etymological correctness. A more elaborate discussion of the chronological development of body section

From the Edward Mallinckrodt Institute of Radiology and the Department of Otolaryngology, Washington University School of Medicine.

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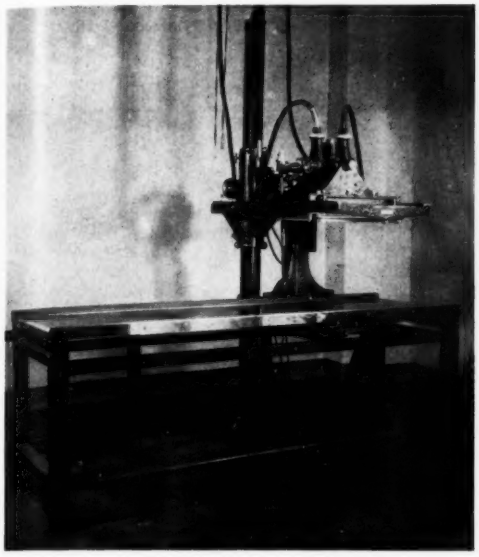

Fig. 1. Photograph of the laminagraph.

roentgenography will be found in the publications of Andrews.

In all body section roentgenography, regardless of the method and apparatus employed, there is the same objective in view. This is to disperse overlying and underlying shadows and leave a selected layer in the body relatively unobscured. Another objective is to visualize as thin a layer as possible because minimal contrast in density in such a layer can be brought out. This is called the "depth of focus" of the apparatus. As a general rule, the more compound the movement of tube and film during exposure, the more efficient the dispersion of unwanted shadows. These two points comprise the fundamental value of body section roentgenography in normal anatomical structures. When pathological states produce abnormal increase of density or the converse, or induce unwanted shadows, body section roentgenography is of the utmost value.

The clinical work which will be presented was done with the laminagraph, which was invented by Mr. Jean Kieffer, of Norwich, Connecticut (Fig. 1). This apparatus differs from all other types and combines all the mechanically possible co-ordinate movements of tube and film, as far as known, and these can be varied as desired. The spiral movement has proved the most satisfactory, and in routine clinical work we have used it almost exclusively. With this movement the laminagraph

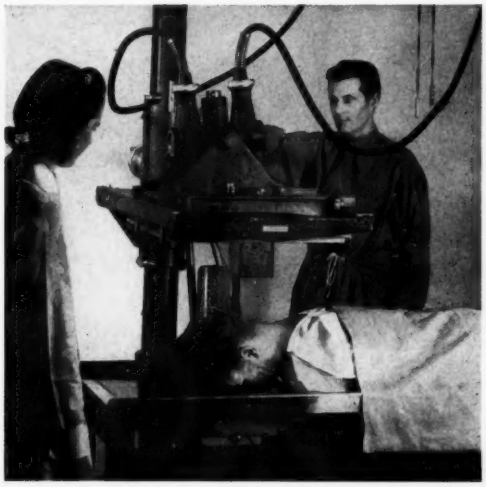

Fig. 2. Position of patient for laminagraphic examination of the paranasal sinuses. Films made at 4, 5, and 6 centimeters from the table top usually suffice.

has demonstrated superiority in the symmetry of its dispersion of unwanted shadows, or blurring. Like the tomograph and its simpler modifications, our apparatus can be used only with the patient in the recumbent position, whereas the com-

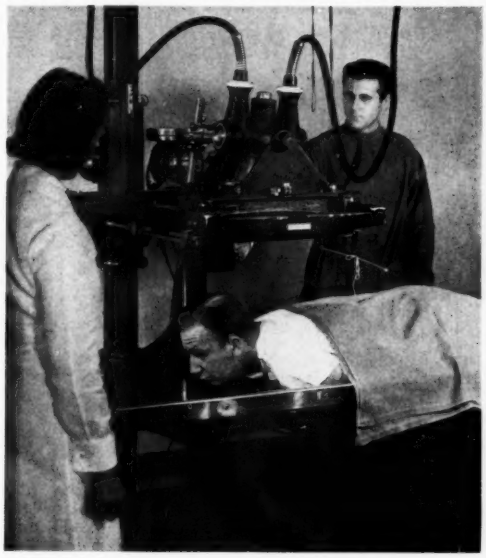

Fig. 3. Position of patient in making laminagraphic examination of the larynx.

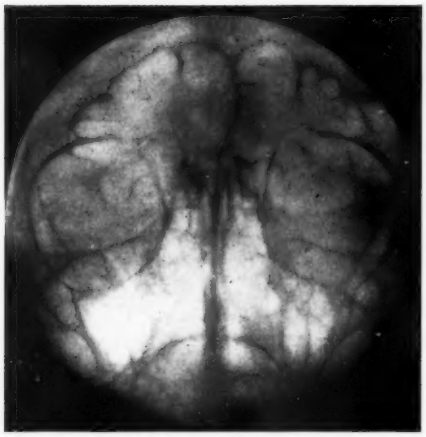

Fig. 4. Case 1, A. S. The laminagram shows extreme supra-orbital extension of an ethmoidal cell. The possibility of this extension has been stressed by Mosher in reference to failures of frontal sinus operations in which the presence of such a cell is not known. Left, conventional film; Right, laminagram at 4 centimeters.

Fig. 4b

mercial planigraph, the biotome, and the stratigraph utilize the erect position.

In considering the clinical applications of this method, one must constantly keep in mind its primary objective, the dispersion of overlying and underlying shadows. It follows that in those regions where there is a maximum of these shadows the method will be of the greatest value.

Fig. 5a

Fig. 5b

(*Legend on opposite page.*)

Fig. 5c

Fig. 5d

Fig. 5e

Fig. 5f

Fig. 5. Case 2, R. L. Supra-orbital extension of frontal ethmoidal cells, marked septal deformity and changes in density in ethmoid and sphenoid sinuses. Second series of films of same patient shows corrected septal deformity with considerable clearing in ethmoid sinuses. There is still some blurring in left sphenoid sinus. a, b, c, Pre-operative laminagrams taken at 2, 5, and 6 centimeters. d, e, f, Postoperative laminagrams at same depths.

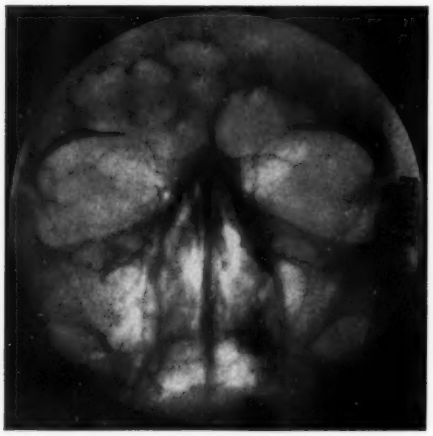

Fig. 6a

Fig. 6b

Fig. 6. Case 3, H. A. The laminagraphic series illustrates wide variations of the ethmoid cells, supra-orbital extension of anterior ethmoids and marked extension or invasion of the maxillary sinuses. a, Conventional film, and b, c, d, e, f, laminagrams at 3, 4, 5, 6, and 7 centimeters.

Unwanted shadows produced by a pathological process have, in our experience, been most frequent in the respiratory tract. In certain of its portions there are a number of normal structures, the shadows of which it is desirable to eliminate, for example the bones overlying the paranasal sinuses, the ribs and sternum in the chest, and the spine in the region of the larynx. It is in this field that body section roentgenography has its forte, and its usefulness has been repeatedly demonstrated by many workers.

In the examination of the chest, of which we have made 410 laminagrams, we have found cavities and consolidation in the lungs which were not apparent either roentgenoscopically or in conventional films. The method has been of little value in early acute disease in the lungs. However, excavation has been shown where there was minimal change. It is undoubtedly true that the absence of grosser changes, such as cavity and consolidation, can be established with the same degree of accuracy as their presence.

The location, size, and physical characteristics of pulmonary cavities can be accurately determined. Therefore, the surgeon, knowing in advance the exact location and nature of the lesion, can plan his approach with assurance.

The laminagraph can clearly reveal the tracheobronchial tree and has revealed bronchial branches as small as 3 to 4 millimeters in diameter. Dislocation, impingement or distortion, and termination through obstruction have been clearly shown. In cases in which carcinomatous infiltration has been diffuse, absence of bronchial branches has been shown, and dislocation of branches in the adjacent, healthy lung has also been revealed. Of course, this applies only to those early cases in which suppuration and abscess formation have not occurred.

In the examination of the paranasal sinuses the problem of superimposed structures has always been troublesome, and 3 years ago we predicted that "laminagrams should aid materially in such conditions as petrositis of the temporal bone, conditions involving the temporomandibular joint and deep-seated paranasal sinuses, to mention only a few anatomical regions." At present, so accurate is the laminagraphic diagnosis of paranasal sinus disease that requests for these films by the otolaryngological surgeons are sent in almost daily (Fig. 2).

The second basic principle of body section roentgenography, namely the thinness of the layer roentgenographed, is important in the examination of the paranasal sinuses because it has bearing on the minimal contrast in density. In the examination of the ethmoid cells laminagrams reveal the size, position, extensions, and other anomalies, and the pathological states far beyond anything possible with standard x-ray procedures,

Fig. 6c

Fig. 6d

Fig. 6e

Fig. 6f

(*Legend on opposite page.*)

however extensively they may be carried out. This is also true of the sphenoid group both in the anteroposterior and lateral projections. The conventional films of the maxillary sinuses generally suffice, but there is the occasional case in which a pathological condition is revealed with laminagrams when it was entirely unsuspected even when contrast media were employed.

Fig. 7. Case 4, J. W. These two laminagrams illustrate marked differences in densities in the ethmoid and maxillary sinuses. The film above is pre-operative, that below, postoperative. Both were made at a 5 centimeter depth. The patient was a child with an orbital involvement secondary to sinus disease.

Fig. 8. Case 5, I. B. This laminagram at 4 centimeters shows a bilateral involvement of the ethmoid sinuses in a patient suffering from bilateral retrobulbar neuritis. The history in this case was previously reported and is included here only because it is our firm belief that laminagraphy will prove to be of the greatest value in patients with posterior sinus disease and serious eye disorders in whom all other methods of examination may be unsatisfactory.

So far we have made no practical application of this method for studying the pneumatic structure of the temporal bone. However, the auditory canals can be revealed throughout their extent in those rare cases of non-development of the auricle. This is the most accurate way of establishing enlargement of the internal auditory meatus in suspected eighth nerve tumors. We have had operative confirmation of laminagraphic findings in 2 cases. Any alteration of the auditory canal, either enlargement through soft tissue growth or decrease in size through bony growth, is discoverable with this method. The presence and the size, or the absence of the groove for the lateral sinus can be shown in adults. However, it is improbable that this would be possible in younger patients because of slight development of the groove, and unfortunately it is in such cases that this knowledge would be of the most value. There is no evidence to suggest that a thrombosis of the lateral sinus can be visualized with laminagrams.

The condition of the articulation of the mandible with the temporal bone can be established by

this method when it is impossible to do so with conventional films because this joint is heavily overlaid by the zygomatic process and other bony structures. Deformities, erosion, and fractures of the condyle and glenoid fossa have many times been revealed, and the laminagraph has proved of great value in the diagnosis and treatment of the "temporomandibular syndrome." This has been reported by Bleiker and by Pippin and associates.

The larynx can be investigated to great advantage by this method as has been demonstrated by Canuyt and Gunsett, in France, Leborgne, of Montevideo, and Howes and Caulk, in this country (Fig. 3). Mobility of the vocal cords can be investigated in different phases of phonation, and deviation of the air columns in the larynx, encroachment on the air passages by new-growth and edema, and increase in its size through ulcerating processes can be clearly shown. This is of particular value in the subglottic region, inaccessible to the laryngoscope. The exact clinical value in the diagnosis of subglottic regions has not yet been established. Leborgne considers this method of great value but properly states that it should be supplemented by direct laryngoscopy and also the lateral standard view of the larynx. We cannot agree to the importance of the latter. In our experience certainly the lateral laminagrams of the larynx have been valueless probably because that structure is too great a distance from the film for this type of examination.

By varying our factors during 3½ years of experience we have worked out a technique for the laminagraphic examination of the paranasal sinuses which has become approximately standard in our clinic. This has been described elsewhere. In general it may be said that standard roentgenography should always precede the laminagraphic examination so that the films may be used as a guide. When the laminagrams are made, the patient is placed in the prone position with the plane of the face parallel to the top of the table. In the routine method, films are made at 4, 5, and 6 centimeters from the plane of the face. This covers the anterior and posterior ethmoid cells and the sphenoids. These planes were established by experimental work with cadaver heads and are, for all practical purposes, accurate. As has been previously stated, the standard film usually suffices in the examination of the maxillary antra, but occasionally laminagrams are needed, not only for the maxillary antra, but also for the frontal sinuses. In that event additional laminagrams are made. For the frontal sinuses these are 0.5 and 1 centimeter, and, if the frontal sinuses have a great anteroposterior dimension, 1½ to 2 centimeters in addition. To cover the maxillary antra laminagrams at 2 and 3 centimeters in addition to the routine 4 centimeter film are sufficient.

Sluder stated, "The x-ray, in my experience, has failed to help in the diagnosis of hyperplastic post-ethmoidal and sphenoidal disease. It is of paramount value in determining cell anomalies, showing probes in positions which determine these "

Cone, Moore, and Dean reported on the relationship of paranasal sinus disease to ocular disorders as studied by laminagraphy. Changes in density of the posterior sinuses and variations in development were demonstrated. Pathological studies of tissue removed and the clinical improvement after treatment suggest that sinus disease is an important cause of ocular involvement.

S. Salinger has informed us regarding a patient with optic neuritis in whom disease of the posterior sinuses was discovered by laminagraphy. Conventional roentgenography was inconclusive. Recovery followed surgical drainage of the sinuses. Weve and Ziedses des Plantes reported a case of optic atrophy and paresis of the extra-ocular muscles due to an isolated lesion in the ethmoid bone which was not seen in the routine roentgen films but which showed up beautifully in the planigraphic studies at a depth of 5 centimeters.

Sluder, in 1927, stated,

> "The frequency of headache without recognizable systemic or organic neurological basis is well known. The mystery of the etiology of many eye lesions is well known. From a very extensive experience with such cases I am led to the belief that their explanation is to be found in the hyperplastic lesion of the post-ethmoidal—sphenoidal district, to a degree of frequency that, could it be put into percentages, would astonish us all, however familiar we may be with such cases. At the same time it must be clearly understood that I do not at all believe that lesion to be the explanation of all such cases."

Today the relationship of sinus disease to ocular disturbance remains controversial. The frequency of optic-nerve involvement in patients with multiple sclerosis is well known. It has been suggested that not only the optic-nerve involvement but also the lesions of multiple sclerosis may be caused by invasion of the nervous system by way of the sinuses. Stark stated, "one (multiple sclerosis) being an advanced stage of the other (retro-bulbar neuritis)."

The improved methods of study of virus diseases and their possible extension by way of the respiratory mucous membrane has been reviewed in the Harvard Symposium (17). It is possible that numerous controversial questions may be answered when more exacting studies are made.

The value of laminagraphy is best demonstrated by the unquestionable information which its use

permits in showing variations in cell development. Interpretation of varying densities of individual cells may remain controversial. The possibilities are shown in the cases which illustrate this text.

In evaluating body section roentgenography it is well to remember that this method must be judged as an adjunct to conventional roentgenography and not as a substitute for it. As such it is an invaluable aid to the otolaryngologist, for laminagrams reveal changes in the sinuses undiscoverable by other methods and should be used if a sincere effort in establishing the diagnosis is to be made.

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TRENDS IN CATARACT SURGERY

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THE vast amount of literature appearing within the past decade is definite evidence that interest in cataract surgery is not waning. It is also proof that steady progress is being made, for while not every article is a real contribution it does show thought and out of so much thought must come some good. For example the presentation of so many variations in cataract sutures, although confusing, has made us realize the desirability of accurate wound closure. Similarly the oft-repeated debate of extracapsular versus intracapsular extraction has led to the realization that each has its place.

Preliminary examination. During this decade our attention has been directed repeatedly to the necessity for careful pre-operative physical study of every patient, although little that is new has appeared. While reporting on postoperative complications Berens and Bogart have pointed out the prophylactic value of such an examination. The pre-operative administration of vitamin C has been advocated by Urbanek and Albrecht on the theory that old patients with cataracts frequently have vitamin deficiencies. More care is taken to control the diabetic and arteriosclerotic patient before operation but in general no great advances have been made.

A necessary part of the complete ocular examination should include a measurement of the intra-ocular tension. This point, which was emphasized for many years by the late John M. Wheeler as a safeguard against the coexistence of glaucoma and cataract, has recently been adopted as a routine measure.

The value of conjunctival smears and cultures as a pre-operative prophylactic measure is still debated. There are some, e.g., Gailey, Herrenschwand, and others, who are of the opinion that they are useless, while others, Elschnig, Kapuscinski, and others, will not operate in the presence of a positive smear—gram positive diplococci—without culturing the organism on bouillon and blood agar plates to determine its pathogenicity. Pre-operative treatment of the conjunctiva is also not standardized. Elschnig and Goar use oxycyanide of mercury 1:5000 and Wright (55) 10 per cent argyrol for one week before operation while others use 0.5—1 per cent silver nitrate or argyrol 25 per cent one hour before operation and still others use nothing but thorough lavage on the operating table. The advisability of pre-operative sedatives seems generally accepted. Those most favored at the present time are nembutal and sodium amytol.

Anesthesia. In addition to the usual instillation of a local anesthetic some form of akinesia is widely used. In 1914 Van Lint described his method of producing a temporary paralysis of the branches of the facial nerve by infiltration anesthesia along the outer orbital margin. After several modifications this was followed by Wright's (56) suggestion in 1923 that the nerve be blocked at its point of emergence from the stylomastoid foramen. O'Brien, in 1929, described his technique for blocking the facial nerve at a point just external to the condyle of the inferior maxilla. The necessity for some form of akinesia is so universally recognized today that it is difficult for us to realize the newness of this safeguard.

The retrobulbar injection is not new, for one finds that Hermann Knapp, in 1884, used it successfully in a case requiring an enucleation. However, its widespread use in cataract surgery is of comparatively recent date. Enthusiastic approval of retrobulbar anesthesia is shared by many but few go as far as McCool and Dickey in believing that "if we were obliged to discard all the measures which we use to safeguard the eye, save one, we would unhesitatingly retain retrobulbar injection." The fear of an orbital hemorrhage has caused some operators to use instead an injection into Tenon's capsule, for example, Stallard. Still others, Hartshorne, for example, point out that satisfactory anesthesia can be accomplished by local instillations and subconjunctival injections. Although orbital hemorrhages do follow retrobulbar injections it is rare, as was strikingly shown by Atkinson. He collected data on 8,000 retrobulbar injections and found only 8 orbital hemorrhages, 5 of which were admittedly due to faulty technique. He correctly urges the use of a 3.5 centimeter needle as a safeguard against vessel injury at the apex of the orbit. Arruga believes that the use of a sharp needle is contra-indicated while Elschnig stresses the importance of quick energetic compression immediately after the injection. Gailey, Kubik, and others think that a slow injection of novocain ahead of the tip of the

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needle reduces the frequency of an orbital hemorrhage. The reduction in intra-ocular tension which follows the injection is the strongest argument for its use in intracapsular extraction and is a definite hindrance to its use in extracapsular extraction. Those operators using the extracapsular extraction exclusively rarely employ it, while those using both methods use it only when the intracapsular extraction is contemplated.

Davis (10), Laval, Spaeth (48) and others have reported the successful use of avertin anesthesia in cataract extraction in unco-operative patients. Graves has advocated paraldehyde anesthesia per rectum supplemented by omnopon. The newer intravenous anesthetics have also been used—Franceschetti, Gil, and Stallard—but the vast majority of surgeons still use a local anesthetic.

Retraction suture. The forceps fixation of the superior rectus as described by Angelucci has been supplanted by the use of a retraction suture under this muscle. This method of controlling the movement of the eyeball has gained in popularity until today it is looked upon by many as one of the necessary safeguards in cataract extraction. Most operators pass a suture through the conjunctiva and the stump of the superior rectus. Graves, however, believes that the conjunctiva should be dissected up and the suture introduced into the tendon alone. Bartels and Wright (56) think that the use of the suture predisposes to prolapse of the vitreous because if too much traction is made upon it in an endeavor to direct the gaze downward a dangerous bulging of the wound occurs. Beach and McAdams, Lowenstein, Saint Martin, Vogt, and others urge akinesia of the superior rectus instead of the suture as the safest method to prevent an upward rolling of the eye. It can be said that some form of control over the upward movement of the globe is very desirable in uncooperative cases. It is true the suture has certain disadvantages but akinesia producing a complete inability to rotate the eye upward predisposes to wound gaping and vitreous loss. It seems logical therefore to introduce the suture and employ it whenever needed. It should be gently held and if the patient does not co-operate satisfactorily not unduly drawn on, particularly after delivery of the lens as this may cause vitreous prolapse (Buxton). The use of akinesia has diminished the frequency of the need of canthotomy, but it is advocated in prominent eyes or whenever the lids exert even the slightest pressure upon the globe in the region of the external canthus.

Incision. The corneal incision is used by a few operators who believe that a conjunctival flap is too bloody (Appleman, Jackson) but the vast majority of surgeons prefer some form of conjunctival flap. Various techniques have been described; some prepare the flap before starting the incision while others make it with the cataract knife and leave a conjunctival bridge. Wright (56), O'Connor, McReynolds, and others advocate the conjunctival bridge in complicated cataracts. It was suggested as a safeguard prior to the use of sutures and while still employed is less widely used now that the value of accurate wound closure is so generally accepted.

Most surgeons still prefer the Graefe cataract knife for making the incision although a few advocate a keratome incision enlarged with scissors. This method has never gained in popularity. In this connection one notices that many cataract sections are made small to insure proper location and to avoid injury to the iris and then subsequently enlarged with scissors—a justifiable procedure whenever one is operating in the presence of a shallow anterior chamber but not with one of normal depth. A section made with scissors is rarely as smooth as one made with a knife. Scattered throughout the literature one finds the recommendation that in the event of the iris coming in front of the knife during the incision the operator should proceed with the incision, even cutting the iris if necessary. Under these circumstances the operator in his endeavor to avoid the iris makes an incision well anterior in the cornea or if the iris is cut has but little control over the shape, size, and position of the coloboma. This teaching was strenuously opposed by the late John M. Wheeler, who believed that the knife should be withdrawn immediately and the section completed with the scissors.

Sutures. As long ago as 1869 Williams advocated suturing the cataract incision, pointing out that by "securing a more immediate union, we not only avoid ulceration of the border of the flap and prolapsus iridis with its attendant evils, but the prompt restoration of the fullness of the globe and of the normal relation of its several parts lessens the chances of irritation from pressure of any cortical fragments or remnants of the capsule upon the delicate contiguous structures and the occurrence of iridocyclitis." In spite of this clear-cut statement, the truth of which is generally conceded today, we find that suturing of the cataract incision has received considerable attention only within the past 20 years. During the past 10 years many variations in technique have appeared and much has been written enlarging upon Williams' dictum. All this has been to good purpose, for it has made the cataract surgeon so suture conscious that today he does not ask if a

suture is necessary, but he does ask which one is best. In 1937 Ellett presented an excellent review of the subject with a discussion of the various types of sutures employed. It is well to review some of the facts set forth by this author, as they show the trend in "sutures for cataract extraction."

The conjunctival suture as initiated by Williams is still widely used. Its chief virtue lies in the ease with which it can be introduced, after the section is completed. Many operators, for instance, Spaeth (48), prefer it for this reason as they want no distracting influence, such as the presence of a corneoscleral suture while making the incision. Since a proper section is so necessary it certainly behooves us to see that the suture does not interfere. If a conjunctival suture is used the flap should be narrow because the elasticity of this membrane is so great that a large flap has practically no splinting effect upon the corneoscleral wound. The experimental work of Hilding is noteworthy, for this worker, using enucleated oxen eyes, made a series of measurements of the intra-ocular pressure necessary to cause prolapse of the iris through limbic incisions under various conditions. From these experiments he concluded that "conjunctival flaps and pockets are essentially ineffective in re-enforcing limbic incisions so as to prevent gaping of the wound and herniation of the iris when healing effects are eliminated." The conjunctival protection of the wound hastens healing but since most iris prolapses occur within the first three postoperative days it is doubtful that the presence of "healing effects" changes the validity of this statement. Leech and Sugar, in their analysis of 450 cataract cases, found that the postoperative complications of (1) prolapse of iris or vitreous or both, (2) delayed closure of the anterior chamber, (3) hyphemia, were much less frequent when sutures were used. The conjunctival suture was found of definite value and the corneoscleral suture of even greater value. Gradual acceptance of the virtues of suturing the wound has led to innumerable variations in technique.

The corneoscleral suture. Since Kalt, in 1894, described the first corneoscleral suture it seems as if almost every ophthalmologist has attempted to devise some modification of it, until today hardly any two surgeons employ the same technique. Kalt's method has many advocates, among them being Arnold Knapp and Ellett in this country, whose vast experiences certainly justify our giving serious consideration to this form of wound closure. Kalt describes the method of insertion as follows: "The suture consists of a vertical corneal portion and a transverse episcleral portion. The whole forms a T with a gap between the junction of the horizontal portion with the vertical portion. The length of each of the portions does not exceed 1 millimeter. The vertical intracorneal branch follows the vertical corneal meridian and stops exactly at the junction of the transparent portion with the sclera. The horizontal portion traverses the opaque part of the limbus as near the cornea as possible. An interval of 0.5 millimeter corresponding to the limbus is ample to permit the passage of the knife." Liegard modified this suture by placing both bites horizontally. This type of suture is strongly endorsed by Stallard (49), Leech and Sugar, and others. McLean recently published a description of an effective corneoscleral suture in which after dissecting down a small conjunctival flap a small slot is made at the base of the flap about half way through toward the anterior chamber. A fine black silk suture is then run through the base of the conjunctiva and then through both the scleral and corneal lips emerging in clear cornea just below the base of the conjunctival flap. The increased efficiency of corneoscleral sutures over conjunctival sutures in reducing the number of postoperative complications has been stressed by many (Ellett; Stallard, Lindner) and statistically shown by Leech and Sugar. Among their conclusions were: (1) the number of postoperative prolapses is reduced and when prolapse does occur it is smaller; (2) the occurrence of hyphemia is reduced; (3) anterior chambers are reformed earlier; (4) prolapse of the vitreous is eliminated. They also pointed out the advantages of greater postoperative freedom to the aged who with this safeguard can be allowed up within 24 to 48 hours after operation.

Today the indecision rests not upon the value of the corneoscleral suture but upon the best time and way to introduce it. One finds many experienced operators who insert their sutures after the section is completed and others who introduce them before the eyeball is opened. The increased sharpness and delicacy of the atraumatic corneal needles greatly facilitate their introduction after the section is made. However, judging from my experience and observation, sutures introduced at this stage are much less accurately placed and sometimes the operator has to be content with a conjunctival closure, or else run too great a risk in attempting to pick up the sclera. The placing of the suture while the eyeball is still intact is safer although its presence tends to interfere with the smoothness of the section. Nothing must be allowed to interfere with the section, but very little is lost if the suture is severed by the knife.

It can be reinserted upon completion of the section just as easily if not more easily than the original introduction.

Iridectomy. The popularity of the preliminary iridectomy has gradually receded, except in England, and today it is used as a routine measure by comparatively few operators. Its usefulness in dislocated lenses was stressed by Wheeler, and as he so aptly pointed out these iridectomies should be broad. Many operators, such as Davis (11), O'Connor, and Gradle, use it only in complicated cases. It seems logical to state that in any case with vitreous in the anterior chamber or when vitreous loss is almost certain to occur its use is definitely indicated.

Although a complete iridectomy at the time of extraction is favored by many competent and experienced operators, notably Knapp, Davis (11), Appleman, and others, the trend is definitely toward extraction with a round pupil. Ellett, Peter, Verhoeff, Bracken, and many others have commented upon the advantages of retaining the iris sphincter. Its presence is said to assist in preventing prolapse of the vitreous in the intracapsular extraction and to lessen the chances for capsular and cortical incarceration in extracapsular extraction. It is generally agreed that an iridotomy or peripheral iridectomy lessens the chance of iris prolapse. Hilding's experimental work, previously quoted, showed that "an iridotomy opening added to the sclerocorneal suture made it almost impossible to produce prolapse when the opening acted well." This would seem to indicate that the opening to be of value must be large enough to permit free passage of fluid from the posterior chamber to the anterior chamber. The increased frequency of iris prolapse when a round pupil is attempted is not universally admitted but the majority of operators definitely feel that such is the case. A careful pre-operative study of the iris and lens may prove helpful in reducing the occurrence of this complication. A loss of resiliency in the iris from sclerosis, atrophy, adhesions, or any cause tends to increase the chances of iris prolapse. These cases in my opinion should have a complete iridectomy. As Wright (56) has pointed out there is increased difficulty in delivering the lens in its capsule or a large nucleus in extracapsular extraction in the presence of a rigid pupil. In this group he favors an iridotomy including the sphincter in preference to a complete iridectomy. Just 10 years ago Lancaster, in an address before this society, stressed the advantages of a basal iridectomy over a complete iridectomy. He believes that a basal iridectomy is even better as a preventive of prolapse than a complete iridectomy, pointing out that it prevents "capsule complications and at the same time avoids most of the iris complications." Within the past decade the truth of these statements has been appreciated more and more until today the complete iridectomy is no longer a routine procedure but is used whenever the operator encounters definite contra-indications to a peripheral one. Even though corneoscleral suturing and consideration of the contra-indications to peripheral iridectomy have materially reduced the number of iris prolapses it is still one of the more frequent complications and its management remains unsettled. Cauterization of the prolapse with trichloracetic acid is advocated by many—Bothman, Gailey, Magitot, Dubois-Poulsen, and Gifford—but others condemn it and suggest excision at the earliest possible moment as the only satisfactory method for curing this condition.

Selection of operation. Probably the most striking change that has occurred in cataract surgery within the past 10 years has been the increasing number of advocates of the intracapsular extraction. The extracapsular method is defended especially by Jackson, Moehle, Wright (56), and others, but the number of experienced operators who routinely use the extracapsular extraction is diminishing. Davis (11), for example, after using exclusively the extracapsular method for 19 years is enthusiastic over the smooth postoperative course of his intracapsular cases. Gradle believes "in the hand of the experienced operator the Elschnig method of intracapsular extraction is just as safe, if not more so, than the older capsulotomy method." On the other hand Pischel after an analysis of a series of cases done by both methods concludes "while the results in the successful intracapsular operation are practically as good as those in the well performed extracapsular operation, there were more bad results even in a selected series of cases of intracapsular operations than in an unselected series of extracapsular operations."

Thus it would seem that the important consideration in cataract extraction is the selection of the proper type of operation. It is not within the realm of this paper to discuss the indications for the intracapsular operation which have been so concisely given by Arnold Knapp who believes, "There is more or less general unanimity in the selection of cataracts that are suitable for this operation." The recent improved methods of anesthesia and other aids have greatly reduced the list of contra-indications. Unfortunately, however, the tendency has become more and more prevalent to attempt an intracapsular extraction

on almost every case. One often hears that nothing is lost if the capsule ruptures and the lens has to be extracted by the extracapsular method—a teaching which in my opinion should be condemned. We have all had the capsule tear after dislocation has taken place and been forced to deliver as best we can a sticky, partially opaque lens. Under these conditions the removal of the cortical matter by irrigation or by mechanical means is not without added risk and the usual result is that a large portion of it remains. It often lies in the upper part of the anterior chamber more or less in contact with the wound. Secondary glaucoma is not an infrequent sequela. The intumescent cataract which is generally recognized as unsuitable for intracapsular extraction is the most frequent cause of this complication. Similarly failure to consider other contra-indications may produce disastrous results.

Within the past 10 years there has been no appreciable change in the technique of the extracapsular extraction, but many articles have been written upon modifications of the intracapsular operation. Without entering into a discussion on the merits of these various methods it is sufficient to say that the technique most frequently employed is the so called forceps and pressure method. No uniformity of opinion exists on the best way to apply the forceps, but the majority believe that they should be used only to control the delivery of the lens which is largely expressed by pressure. Some (Knapp, Peter, Elschnig, and others) insist upon tumbling the lens while others (Beach and McAdams and Verhoeff) apply the forceps above in the equatorial region and extract the lens head on. The eresiphake, as designed by Barraquer, has its advocates and many modifications of this instrument have appeared but its use has never become widespread. Saint Martin suggests that it is ideally suited for the intracapsular extraction of the intumescent cataract in which the forceps method is so often unsuccessful—a thought worthy of further investigation, for if we could succeed in extracting these lenses without rupturing the capsule much trouble would be averted.

Wright (56) with an enormous experience of over 20,000 cases correctly sums up the situation in these words, "Dogmatism in connection with the various procedures of the operative treatment of cataract is not uncommon, as one may judge who follows up current literature, but the greater one's experience the more inclined one is to adopt an open mind. A man may indulge in dogmatism when he has collected figures in connection with 100 cases of the operative treatment of cataract, but he will be less inclined to do so after his thousandth extraction and completely alter many of his previous views after his five thousandth case." There are few if any of us who will ever perform such a vast number of cataract extractions. Nevertheless the truth of this statement can not be denied. Let us, therefore, realize that there are indications for the extracapsular as well as for the intracapsular extraction and strive constantly toward a perfection of these indications.

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THE 1940 CLINICAL CONGRESS

THE COLLEGE AND AMERICAN SURGERY

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A PRESIDENTIAL address in my opinion should give an account of the affairs of the organization, an accounting for stewardship as it were. The American College of Surgeons is fortunate in having a splendid organization with minute and detailed reports available, and hence its president has but little to do. Therefore, it seems to me that this address might serve to welcome the initiates who shortly will become Fellows of the College and also to discuss certain details of the College, its aims, and objectives.

Most of the successful ventures in human endeavor come from organization and we think this is particularly true of medicine. The labor union exists for the purpose of improving the economic status of its members; the medical association or college exists to improve the scientific attainments of its members by organized effort.

The foundation of the American College of Surgeons sprang from an idea. In 1903, the Society of Clinical Surgery was organized for the purpose of demonstrating to a group of surgeons the methods used in different leading clinics. The effort was most successful and naturally as surgeons from different cities watched each other work, they were bound to carry home with them the best of the surgical procedures they had observed. Apparently this gave to Franklin Martin, of Chicago, the idea of organizing a greatly magnified and practical clinic.

In 1910, in Chicago the Clinical Congress of Surgeons of North America was organized, and 1,300 surgeons were in attendance. The organization was rather loose and Martin, with characteristic foresight, saw the possibility of banding these men together in an organization which would stand for the uplift of surgical principles and technique and practice. Hence, he formulated the organization of the American College of Surgeons in 1913, and after a founders' group had been formed, 1,059 initiates were enrolled into fellowship at the first Convocation.

Presidential address of the retiring president, presented before the Clinical Congress of the American College of Surgeons, Chicago, October 21–25, 1940.

In the Articles of Incorporation it is stated that the object for which the American College of Surgeons is formed is

"to establish and maintain an association of surgeons, not for pecuniary profit but for the benefit of humanity by advancing the science of surgery and the ethical and competent practice of its art; by establishing standards of hospital construction, administration, and equipment, and all else that pertains to them; by engaging in scientific research to determine the cause, nature, and cure of disease; by aiding in better instruction of doctors; by formulating standards of medicine; and methods for the improvement of all adverse conditions surrounding the ill and injured wherever found. To accomplish these benevolent and charitable aims, it shall be within the purposes of this corporation to use those means which from time to time may seem to it wise, including research, publication, education, the establishment and maintenance of libraries, museums, and other agencies or institutions appropriate hereto, and the co-operation of any other such activities, agencies, or institutions already established or which may hereafter be established."

Whoever wrote these sentences wrote a masterpiece because in the twenty-seven years since its organization the College has done every one of these things.

The historic position of the early beginnings of the American College of Surgeons is somewhat different from that of other colleges then in existence. Conforming to the democratic principles of this country, its fellowship was considered inclusive, not exclusive, and it was to be conferred upon surgeons of character, honesty, and ability without particular regard for examination. Certain simple standards were set up, but the supreme test was the recognition of the candidate's fitness by a group of surgeons, Fellows of the College, who knew him best because they worked together in the same community. Therefore, from the beginning the opinion of the State or Provincial Credentials Committee was the dominating influence against the admission of those known to be incompetent or unethical.

It is not so difficult to judge a man's knowledge of the theory and technique of surgery by examination as it is to know that he can apply this knowledge to the individual patient; it is important to know that the surgeon is able to work in a community without friction with his colleagues,

and it is most important to know that he is honest in his relations with the patient. The College makes every effort possible to combat the evil of fee-splitting and while it may not be an issue in all communities and in all hospitals, it has been necessary to establish a uniform regulation to avoid discrimination and to require the medical staff and governing board of every hospital desiring approval to go on record against this practice. Once on record, it is the duty of the hospital management to exercise continuous vigilance to prevent fee-splitting under any guise. The pledge against the division of fees, which is signed by all initiates, was proposed by Dr. Albert Ochsner in Chicago in 1913.

The meeting held each fall is the high point of our College year. The program consists of papers and discussions, of clinics and operations, all illustrative of the progress of the surgery of the day. Those who formulate the program endeavor to give the meeting the benefit of the master minds of surgery. If you would take the time to examine the Clinical Congress programs through the last twenty-seven years, you would read an epitome of the progress of surgery in this country.

In 1920, the College began to organize three or four sectional meetings in different parts of the country each year. They have grown in time so that they almost rival the fall meeting and have been of immense aid in establishing contact with the Fellows of the College.

In a way these meetings are something like other medical meetings, except that they are better, and hence, it is necessary to look further for the great influence of the College. When we do so, we realize that we are part of a great organization exerting a power by the force of our numbers for the good of surgery. If for no other reason, you should be satisfied with your fellowship because, after all, that which concerns the good of surgery as a whole concerns each one of us.

At an early date it was recognized that the hospital and operating room were the laboratories of the surgeon and that many hospital organizations were careless regarding the equipment, the records, and the laboratory facilities. By 1917, the hospital standardization program was well under way and despite the hectic years of the World War our program was developed and a minimum standard for hospitals was adopted in December, 1917. Beginning in 1918, the College began a survey of the hospitals of the United States; these surveys have been made every year since until over 3,600 hospitals are now on the survey list and are regularly visited by members of the College staff.

In 1913, at the suggestion of Dr. Thomas Cullen, of Baltimore, a cancer committee was appointed that subsequently formed the nucleus of the American Society for the Control of Cancer. Later the College took over the bone sarcoma registry and in 1922 began assembling data of all cancer cases living five years or more after treatment. The College then established a minimum standard for cancer clinics and organized them in approved general hospitals. Today there are 345 approved cancer clinics.

In the same year, under the guidance of Dr. Charles L. Scudder, of Boston, exhaustive studies of the present treatment of fractures were conducted and the central fracture committee and regional fracture committees in different states and provinces have become one of the most important duties of the College.

In 1926, we organized a board on industrial medicine and traumatic surgery, which concerned itself with adequate scientific and ethical care of the ill and injured in industry; and this committee, although now fused with the fracture committee, has had a beneficial influence and has made many contacts with the large industrial concerns.

From the beginning, Canada was included in the organization of the College; and in 1920 and subsequent years, Drs. Franklin Martin, William J. Mayo, Thomas Watkins, and others visited the various South and Central American countries, thus binding the surgeons of these countries to the College so that it could be said to be representative of both Americas. As a result of these contacts and because of the standardization program of the American College of Surgeons, Dr. Francis P. Corrigan, now the United States Ambassador to Venezuela and an enthusiastic Fellow of the College, paid a great tribute to the College in his article, *El Libro del Hospital Moderno*.

The influence of the College was recognized during the first World War when President Wilson appointed Dr. Franklin Martin one of seven civilians to the Advisory Commission of the Council of National Defense. This year Dr. Evarts A. Graham, president-elect of the College, has been appointed chairman of the National Research Council Committee on Surgery in connection with the program of military preparedness. The chairman of our Board of Regents, Dr. Irvin Abell, has been appointed chairman of the Committee on Health and Medicine of the Council of National Defense. At the Clinical Congress held in October, 1917, the program was indeed a "war session"; and while we are not at war, you will notice from the program of the present meeting that we are preparing for defense.

It is interesting to me to note the duplication of thought about the two wars. The high point in the treatment of wounds in 1918 was the Carrel-Dakin irrigation; today it will be sulfanilamide. There will be many improvements in transportation, but I think that the basic surgery will be comparable. There is not a great deal of information in the medical literature of the past year regarding the surgical aspects of the war; yet all surgeons liable to service in the event of war prepare themselves by searching every available source for information regarding the treatment of wounds and other war casualties and the hazards of industry in the conduct of war. As a matter of fact, in a total war, every doctor and every hospital is an integral part of the defense plan.

In his presidential address of last year, Howard Naffziger compared medical progress to a growing stream, the first spring feeding it arising in the far distant past until with the development of modern scientific medicine the stream has become a great river. I do not think it possible to say when and where surgery began because no doubt from the dawn of civilization and even before men attempted to alleviate suffering and injury by some form of material help. At any rate, we do know that much of the practice of surgery began in mystery and magic.

The earliest surgical operation which history records was the trepanning of skulls for the release of demons, presumably the epileptic seizures of the present day. Bloodletting began as a ceremonial procedure. Circumcision was practised in 4,000 B.C. according to the picture record and the records in Genesis. In time superstition in medicine disappeared but, despite the enlightening developments of Galen and Celsus, surgery remained in the doldrums until Vesalius early in the sixteenth century taught true anatomy.

Often we hear of an attempt to distinguish between the art of medicine and the science of medicine. Actually, medicine is not a science but gathers its basic knowledge from true science and applies it to the cure of disease; and hence, after Vesalius, anatomical thought ran like a red thread through all of the developments of medical practice. In 1628, eight years after the landing of the Pilgrims, William Harvey announced the theory of the circulation of the blood; thenceforth physiology was inseparably associated with anatomy and surgery became more exact. Harvey taught that speculation alone was valueless; that advances in knowledge would result only from patient experiment, patient measurement, patient application of the method of trial and error; and that the facts, if they were facts and if there were enough of them, would always speak for themselves. Patiently through the years the science of physiology unfolded its secrets to medicine until today we constantly talk in details of function, and surgery endeavors to restore normal function or to remove an offending organ.

Sometime in the eighteenth century the pupils of the great chemist, Robert Boyle, discovered the different gases in the atmosphere and this led to the discovery of inhalation anesthesia, the word "anesthesia" having been invented by Oliver Wendell Holmes. In 1584, Fracastorius wrote that contagion is infection passing from one individual to another. Step by step the picture was completed with Holmes, Semmelweis, Pasteur, Koch, and Lister standing out in the foreground. From the time when Lister developed the technique of antisepsis in 1865, surgeons were concerned with methods which combined antiseptics and sterilization by heat and allowed operations to be undertaken safely with ever increasing freedom.

For a long time there was not much progress except the perfection of details for fulfilling the doctrine of antisepsis. In 1910, Ehrlich produced salvarsan and this discovery not only revolutionized the treatment of syphilis but exerted such a stimulus to chemotherapy that today most progress in surgical technique is closely allied with the progress of chemical research.

Surgery benefited from the field of physics when in 1895 Roentgen discovered x-rays. The efficiency of this instrument of diagnosis and treatment has progressed until today, judging from reports which we hear, we may be on the verge of extraordinary developments by the use of the cyclotron. After Roentgen came the Curies and the isolation of radium, and its use particularly in cancer was another step forward.

These few remarks are introduced merely to furnish a backdrop to the stage on which is played the drama of medical progress. Scientists have discovered so much and the application of their discoveries have complicated medicine so that specialization has developed. For a long time physicians combined the art of general practice with the practice of a specialty. But with the great advances in medicine and science we have come to realize that major surgery is a complex procedure, requiring not only a knowledge of technique but a sound understanding of the principles of anatomy, physiology, pathology, chemistry, and physics.

In the past special training was obtained largely through the personal initiative of the physician.

A period of study abroad was considered necessary and Paris, Berlin, and Vienna were popular meccas for medical students. Courses were given in this country by certain postgraduate schools, but with the exception of the one at the University of Pennsylvania established in 1919, these courses were largely short in duration and rarely satisfactory. Most surgery was taught by the preceptorial method. The younger men became associated with established surgeons as assistants and gradually learned the technique of surgery. As the technique of surgery became magnified, it was realized that the training of the general surgeon and the surgical specialist would require more time and effort on the part of the individual. For many years there have been opportunities for surgical training in the medical school hospitals and in a few other institutions, but it was becoming apparent that the need for training exceeded the good available opportunities. The College realized that in its hospital standardization surveys it had the machinery to increase the opportunities for graduate training in surgery and the surgical specialties. The subject has received the continuous consideration of the Board of Regents since 1930 and several committees have studied the problem in its relations to the requirement for fellowship. During the past three years the committee on graduate training in surgery and the field staff of the College have done a great piece of work and we can announce that 200 hospitals and other medical institutions are participating in approved plans of graduate training in general surgery and the surgical specialties at the present time.

It is interesting to philosophize on the question as to what is a surgeon. In his presidential address read before the American College of Physicians last April, Dr. O. H. Perry Pepper attempted to answer the question, "What is an internist?" He found himself involved in a quagmire of words and meanings and definitions and finally concluded that

"an internist is a physician fitted by a sound and applicable knowledge of the basic sciences, a continued training in clinical medicine, a familiarity with fields outside his own, and an intellectual, rather than a manual or technical, approach to study, diagnose, and treat the diseases of the field of internal medicine to which he strictly limits himself, and to integrate with the knowledge of his own field that of the allied specialties."

With some change in phraseology this definition might define the surgeon. Much of surgical procedure is done, and rightly so, by the general practitioner, but a borderline is soon approached when the performance of a major operation on the brain, the chest, the abdomen or the extremities involves not only manual skill but also a knowledge of anatomy, pathology, and the other basic sciences together with a group of the increasingly difficult problems of pre-operative and postoperative care. The surgeon, therefore, cannot be a general practitioner. He must have time to read, to study, and to observe the work of other surgeons and unfortunately cannot cultivate the personal and family psychology of the patient as can the general practitioner to whom he is consultant and ally.

The formation of the boards of certification has influenced the desire for residencies, and the trend of present opinion is that such a residency is necessary for adequate training in surgery.

"There is gentle irony in the fact that men who to a large extent were self-taught believe that their successors cannot achieve an education in the same manner."[1]

One of the problems of the future should be a study of the effect of prolonged residencies on medical education, on hospitals, and on the practice of medicine. This movement is formulating a very difficult problem for the hospitals because much of their organization must be dislocated in order to accommodate the new and important links between the interne group and the visiting group. Staff members and boards of trustees must be convinced of the importance of the residency and must be persuaded that sacrifice may be necessary to make it effective. The senior visiting staff must assume a preceptorial attitude and regard themselves as graduate professors of surgery. The junior visiting staff is in danger of being squeezed out from above and below unless the adjustment is made so that they also take part in the training plan.

In due time the new system will produce more highly trained men. A present day problem as well as one for the future is to formulate methods or backgrounds that will enable the individual trained in the residencies for two, three, or four years to adapt himself to competitive medical practice. As the *New England Journal of Medicine* states, these men will start with a strong tendency toward group medicine rather than toward individual practice.

I think that now I have said enough and really have said little, but perhaps have offered some points for analysis. In 1874, Sir John Erichsen stated that "the abdomen, the chest, and the brain would be forever shut from the intrusion of the wise and humane surgeon." Unlike Lister he failed to envision the effect of Pasteur's germ theory upon the surgical operation. The researches

[1] Editorial. New England. J. Med., 1940, 222:1022.

in chemistry today seem to us to be revolutionary in their effect upon the treatment of disease, but our sons and our grandsons will develop other ideas which will be thought to be the extreme in modern methods. Unlike Erichsen, we must not exclude any lesion or organ as immune from surgical attack. And then we might look forward to the time when medical science has progressed to the point when all surgery of a destructive type can be abolished.

MEDICINE IN THE NATIONAL DEFENSE PROGRAM

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SINCE the members of the American College of Surgeons, with the exception of the Canadians present, are practically all members of the American Medical Association, I felt that you would be interested in knowing of the work of its Committee on Military Preparedness. This committee was appointed at the session of the House of Delegates in New York in June following a request of the Surgeons General of the Army, Navy, and Public Health Services that the American Medical Association undertake a survey of the profession of the United States regarding the qualifications and availability of its members for service.

There are 179,000 doctors entitled to practice in the United States by means of legal registration, and a questionnaire was sent to each of these. Between 140,000 and 145,000 are in active practice, while the remainder have retired because of age, disability, or their having sought other pursuits. So far 115,000 replies have been received, of which over 50,000 have been transferred to punch cards. These punch cards contain the information furnished by the questionnaires and by using them in the International machine, one may in a few minutes get a list of men qualified in any branch of medicine. This work has been undertaken by the American Medical Association as a patriotic contribution to the National Defense Program and has entailed the employment of an additional sixteen persons in the American Medical Association office. It is hoped that within two or three months information will be at hand upon every doctor in the country. The only exemption in the Selective Service Act applies to students of theology and accredited ministers of the gospel. Deferments will be made to students in accredited schools, pursuing a course of study leading to a degree in Arts and Sciences and also to those who occupy essential positions in their community. In order effectively to safeguard the health of the population and to furnish medical service to the armed forces, the medical profession feels very strongly that medical students should be permitted to finish their undergraduate education and, at least, one year of interneship before being inducted into service. The Selective Service Act, however, provides deferment for students only until June, 1941; after that date any deferment granted to medical students, to internes, and to residents will be the responsibility of the local draft boards. While doctors should be willing to make such adjustments as may be needed in the event of an emergency, it would be unfortunate if in the defense program the classes of medical schools, the teaching program of medical schools, and hospital service should be disrupted by an undue number of students, of internes, and of residents being called into service. This can be avoided only by applying to the local draft boards and to the appeal boards for the deferment of those essential to these three activities.

There are approximately 15,000 members of the Medical Reserve Corps and these will be largely drawn upon to furnish medical service for the first increment of selectees. It is estimated that by July, 1941, the total strength of the army will be approximately 1,400,000 men, for which the services of 10,000 doctors will be required. The length of service of the vast majority of doctors will be one year, at the end of which time they will be transferred to the Reserve Corps on an inactive status. The information being gathered by the Military Preparedness Committee of the American Medical Association will make it possible to employ the services of doctors in position for which their training and qualifications fit them, and thus to avoid some of the mistakes and misfits of the first World War.

Presented before the Clinical Congress of the American College of Surgeons, Chicago, October 21–25, 1940.

The major objectives of the survey are to provide medical service for the armed forces, to provide medical service for industrial mobilization, and to provide continuing medical service for the civilian population. In the first World War more than 32,000 physicians voluntarily served with the armed forces. In the event of war coming to our country again the profession will similarly give of its members a sufficient number to meet the needs of the Army, Navy, and Public Health Service. Furnishing medical service to the rapidly expanding industrial plants presents many difficulties; it will be no task to supply doctors who are fully competent to care for industrial injuries, but it is quite another problem to supply doctors familiar with the toxicological problems of industry. Practically all of the metals, many of the solvents, benzol, tuluol, and many chemicals used in industry are capable of producing rather disastrous toxic effects upon the human organism. To control these hazards effectually requires the co-operation of the physician who is familiar with the problems and the safety engineer who understands methods of prevention. Continuing the service to the civilian population through hospitals and through men in various fields of practice is essential if the health and welfare of the civilian population is to be protected.

On September 19 President Roosevelt appointed a Health and Medical Committee, a sub-committee of the National Defense Council; its members are Surgeon-General Magee of the Army, Surgeon-General McIntire of the Navy, Surgeon-General Parran of the United States Public Health Service, Dr. Lewis H. Weed, chairman of the Division of Medical Sciences of the National Research Council, and your humble servant, representing the civilian profession. The duties of this committee are to advise the National Defense Council on health and medical matters affecting National Defense and to co-ordinate all health and medical efforts. The medical division of the National Research Council has at present 38 committees, each studying some problem in its relationship to military medicine, such for instance as shock, chemotherapeutic treatment of wounds, blood transfusion, aviation medicine, tuberculosis, neuropsychiatry, nutrition, etc. The Health and Medical Committee has appointed sub-committees on dentistry, medical education, hospitals, nursing, industrial health and medicine, and negro health. In all of this work an effort has been made to secure the advice and help of those whose qualifications in their respective fields entitle them to serve with advantage to the country.

It gives me much pleasure gratefully to acknowledge the unanimous offer on the part of the profession at large, of the various national and special medical societies, of the hospital groups, in fact, of all agencies relating to health and medicine to co-operate fully and freely in the defense program.

THE CIVILIAN SURGEON IN WAR

Brigadier General RAYMOND F. METCALFE, M.D., F.A.C.S., Washington, D. C.

BEFORE proceeding with a discussion of conditions in the Army which the civilian surgeon would encounter in the event of a general mobilization, I should feel remiss if I failed to pay tribute to the brilliant accomplishments of a few of our Army medical officers: Major Walter Reed and his associates showed us how to control and practically eradicate yellow fever. Colonel F. F. Russell, encouraged by Surgeon General O'Reilly, with great persistence and hard work secured volunteers to submit to antityphoid vaccine, proving it worthy as a preventative, and thus typhoid fever was practically eliminated from the Army where formerly it took a greater toll of death than battle casualties. There are many young medical officers in the Army today who have never seen a case of typhoid fever. Surgeon General William C. Gorgas, through his knowledge of sanitation and prevention of yellow fever and control of malaria, made possible the construction of the Panama Canal. The work of Colonel William L. Keller in the first World War on empyema cases following wounds and pneumonia is the real basis for all the brilliant present day thoracic surgery. Colonel Keller contributed another important contribution to war time equipment—the "Keller half ring splint," which has completely replaced the Thomas splint in the Army. The Keller splint is reversible and can be used on either right or left leg. After the splint has been padded, the damaged leg is laid in it and the half hip ring is completed to a full ring by a strap. The Thomas splint with a full hip ring can be used only on one side, thus twice as many splints are required. They are much more awkward to store and transport, are more difficult to apply as the injured foot and leg have to be passed through the ring, thus causing unnecessary manipulation of fractured bones.

From the Surgeon General's Office, U. S. Army.
Presented before the Clinical Congress of the American College of Surgeons, Chicago, October 21–25, 1940.

Since this paper was written, early in August, 1940, a considerable portion of the National Guard has been mobilized for defense of the United States. Usually the Guard is called by regiments and the medical officers and enlisted men of the medical department are included. If one million men are mobilized by the selective draft that means seven thousand medical reserve officers will be called for service.

Many of the medical men here served with the Army during the first World War and are familiar with service conditions, and while we all hope that war will not be forced upon us the best insurance against such an event is a well trained and equipped army. I do not believe we will have to maintain a regular army of two million men permanently. Yet, we should have five to ten million men trained in the use of small arms and field guns; airplane pilots; tank drivers; machine gunners, signal corps men; and trained x-ray, laboratory, pharmacy, and dental technicians, as well as men trained in administering first aid.

The only way this can be accomplished will be by the establishment of a selective draft or universal service. The latter is the more equitable method. Every youth from 18 to 21 years of age, physically qualified, could, with advantage to himself and the Government, give 1 year to the Army, Navy, or Marine Corps, and thereafter for a determined number of years serve 14 days yearly with the colors.

If you could observe some of the recruits—awkward, with ungainly walk, round shouldered, and with faulty and unsanitary habits—after a 6 weeks' training period change into upright, alert, self-reliant, and well disciplined young soldiers, I am sure you could not offer a legitimate objection to the selective draft or universal service. Their improved health and physique more than offset any interruption to education; their improved physical condition and response to discipline work to their benefit throughout life. After a few years of

this training, with the spirit and intelligence of the American youth, it would be a bold people who would start trouble with the United States.

The younger medical officers assigned to duty with troops must remember that most of the recruits and draftees face a complete change in their mode of life; their army life is regulated and the change in their habits is very marked. They are awakened by a bugle call, have a very short time to wash, shave, make up their beds, take a setting up drill, go to breakfast shortly afterward, are called to drill again, and this routine continues during the day. At night they are summoned to quarters with a call for lights out at 9:00 P.M. With this regulation of his life, the recruit may neglect the calls of nature and feel ill. The sergeant puts his name on sick book and when sick call is sounded he and others of his company are marched to the doctor's office at the dispensary or hospital. With a large number of recruits, 50 to 100 men may have to report to the medical officer whose duty it is to see each man and find out his complaint. The sergeant, of the medical department, is instructed by his superior officer to take temperatures when indicated, to examine an injury, or otherwise take care of the men. To many a dose of salts will be prescribed, to some a cough mixture, and these recruits will be marked "duty." Some will be detained until the doctor can examine their abdomens; since by change of habits many men become constipated, we must always be suspicious of appendicitis and must not give cathartics when a man has pain in the abdomen. Again, the chest must be examined, and it must always be remembered, that, with recruits from country districts especially, measles, mumps, and meningitis must always be watched for and the men isolated in the hospital, for it is better to isolate them on suspicion of an infectious disease than to wait for many others to be exposed.

The line officers and drill sergeants who are responsible for the efficiency and the discipline of the recruits often speak sharply and with a good intentioned oath. Sometimes the new medical officer trys to emulate his brother officer of the line, thinking the recruit is malingering; and often the new soldier is not seriously ill, just tired, a little constipated, and homesick. The medical officers should be firm but kindly. A little sympathy and friendly advice will help a lot. If there is any doubt of illness, better err by sending the man to quarters or the hospital for a day than to wait until he becomes seriously ill. Remember, the medical officer and the chaplain are the only officers who can show a little sympathy for the new soldier without lowering discipline. Also remember, that, with large concentrations of men, measles is often the first serious condition, followed by pneumonia, then empyema. This disabling sequence may be stopped by prompt isolation of the measles patient.

The American Medical Association has rendered a splendid service by card-indexing the physicians and surgeons of this country with their specialties and qualifications; this index will enable your Government to call on those needed for various assignments. It is often a hardship on a medical man temporarily to leave his practice; yet it will be necessary for all of us to help the Government maintain itself, and I am sure no American born or any adopted by America would care to give up his privileges and opportunities to lead the life he has choosen for that of a totalitarian form of government.

In war the country is divided into zones. That portion where fighting occurs, both land and water, is known as the combat zone. Behind this section, where supplies are brought forward and wounded taken back, is the zone of communications, and farther back, the zone of the interior, where conditions are more or less normal except for the busy factories making supplies for the Army, recruiting, and distributing supplies and caring for the sick and wounded.

The first medical installation in the combat zone where the wounded may receive medical attention is the battalion aid station. This is close behind the firing line. Here, the battalion surgeon with meager equipment can apply a splint to a damaged arm or leg, give a hypodermic of morphine, antitetanic serum, apply a tourniquet and a moderate sized dressing.

Behind the battalion aid station are 3 collecting companies, each with 1 medical officer and 31 litter bearers. The non-ambulant wounded are carried by litter to the collecting station, preferably located behind a ridge or behind wooded land, where they will be protected from direct gun fire. To this point the ambulances proceed and take 4 litter patients or 2 litter and 6 sitting patients per ambulance. The ambulances take their patients to the clearing station; here are 6 medical and 1 dental officer with 95 medical department enlisted men. Also, there is a moderate equipment of field operating tables, medical chests of dressings, instruments, splints, equipment to furnish hot drinks, warm blankets, intravenous fluids. There is also equipment for such emergency operations as removal of hopelessly shattered arms and legs, removal of tourniquets and ligating vessels, application of more substantial splints to fractured arms and legs, removal of cloth or foreign material from sucking chest wounds, suture of the skin and fixation with adhesive straps, adjustment of bandages, suture of gaping abdominal wounds and, if the bowel is perforated, exteriorization of the loop and the application of dressings.

This station is equipped with the following anesthetics: inhalants, ether; intravenous, pentothal sodium; infiltrating, procaine and novocain; local, cocaine for eye and mucous membrane.

The commanding medical officer will have to estimate the patient's condition and decide where he is to be evacuated. At this time I wish to mention the work in 1936 of Major Sam Seeley with Drs. Essex and Mann (1) of the Mayo Clinic. When animals were given ether anesthesia and the peritoneal surface of the bowel was irritated by rubbing with gauze, they went into shock in 3 to 3½ hours. When these animals were given pre-operative sodium amytal, shock was delayed 10½ hours. We have observed in our spinal anesthetics, which are all preceded by sodium amytal or nembutal, that we rarely have a shocked patient. With this observation and the result of the animal experiments mentioned, we recommend that the battalion surgeons and hospital corps men be equipped with sodium amytal capsules 0.2 gram and 1 capsule be given to every seriously wounded soldier before he is started to the rear. If shock is delayed 10 to 11½ hours, the safe evacuation by air or ground ambulance to fixed hospitals in the rear will mean the saving of many lives. Even shocked patients will not recover unless their surgical conditions are corrected. The next station is the evacuation hospital. Here débridements and all type of regional surgery can be done. If a patient can stand ambulance transportation, he should be sent to the evacuation hospital. For the more seriously injured the ideal method of transportation from the clearing station will be immediate evacuation by motor ambulance to a landing field, thence to the base or general hospitals in the zone of the interior by airplane ambulance. A dying man should not be removed from the clearing station.

Translation of "Casualty Evacuation by Airplane" in the Army Medical Bulletin No. 53 (2), based on German experience in Poland, is interesting, as it is probably the first time that battle casualties have been evacuated by air. Lieutenant General Erich Hippka, surgeon general, German Air Force, reports that 2,500 patients were evacuated by plane from Poland to hospitals in Berlin and elsewhere.

Ordinary commercial passenger planes were used. The plane is easily arranged for litter transport by straps and brackets to steady litters. An experienced medical officer in charge and available oxygen is required. The recumbent position lessens danger of air sickness; this rarely occurs under an altitude of 1,000 meters and if greater altitudes are necessary, oxygen relieves. No prolapses of organs or marked disturbances of peripheral circulations were reported. A final opinion of transportability of thoracic injuries was not rendered. Brain and face wounds, eye injuries and shattering wounds of spinal column, pelvis, and extremities were particularly favorable for air transportation *before* operation. Dysentery and typhoid patients were transported by air to home hospitals. Motor ambulance transport is necessary at the front and the home base to and from landing fields. The return journeys of the planes carried sera, medicines, and required equipment to the

front. Of the 2,500 evacuated by plane, only 4 patients died in plane or immediately after landing, and these planes were not staffed by medical officers. The speed of the ambulance planes was maintained at around 144 miles per hour. All planes were in radio contact with a directing center. The rapid evacuation by airplane had a splendid psychological effect on the wounded.

The medical officer at the clearing station has another difficult problem to decide, as many men with minor injuries and feigned illness will drift back to this station. A dressing, a hot drink or stimulant, and a short rest will straighten out this patient and then he must be sent to join his fighting companions. The surgeon must be firm and decisive, as battles are not won by evacuated soldiers.

The evacuation hospital is equipped for all types of emergency surgery and staffed with operating teams assigned to regional surgery, as thoracic, abdominal, cranial and neural, orthopedic, genito-urinary, and plastic maxillofacial. All the usual anesthetics can be supplied at this hospital. During and after a battle, relieving teams, working night and day, care for a large number of wounded. These hospitals are located at a railhead or on a waterway and evacuate the sick and wounded as soon as patients can be safely moved to the fixed base and general hospitals in the zone of the interior.

An interesting report from England in the treatment of wounds of the extremities is that the wounded extremity is carefully débrided, sprinkled with sulfanilamide crystals, bandaged, and the extremity put in a plaster cast; the patient is evacuated and the cast is not disturbed so long as the patient's condition is satisfactory. The results so far reported are excellent. This treatment should be instituted at the evacuation hospital.

One of the newer developments of the medical department is the trailer hospital which was constructed under the supervision of Colonel Garfield McKinney, M.C., at the Field Service Laboratory at Carlisle Barracks, Carlisle, Pennsylvania; and at the request of Colonel McKinney, the surgical staff at the Walter Reed General Hospital and I planned the equipment.

The trailer operating room (Fig. 1) has a floor space 11½ by 7½ feet, storage space in the forward part for instruments, anesthetics, drugs, etc., a scrubbing sink, an instrument sterilizer, ample ceiling light facilities, 4 double plate glass windows each side, walls and ceilings insulated with 2 inches of dry zero, heating and cooling equipment, and a 120 gallon water tank in the forward part.

In supplying the instruments, the various specialists at the hospital were asked to select necessary instruments and omit unnecessary types. We selected a basic set with which most general surgical operations can be done. Then we selected supplemental sets to cover the regional operations. The supplemental sets are abdominal; thoracic; ear, nose and throat; eye, orthopedic; genito-urinary; anoscope; and cranial and brain. There are 4 basic sets and 1 each of the supplemental sets with each trailer operating room. These same basic and supplemental sets will be furnished to all Army hospitals. At the base and general hospitals, power driven instruments for orthopedic and skull cases will be furnished to supplement the basic sets and, of course, all types of anesthetics will be available.

The anesthetics for the trailer operating room are the less bulky types: inhalants, ether; spinals, novocain, nupercaine, spinocaine and pontocaine; local infiltrating, procaine; cocaine for eye conditions; rectal, avertin. The Heidbrink Gas Machine Company, working with Captain William W. Nichol of the Medical Corps, has developed a small compact gas machine to supplement avertin and spinal anesthetics. Due to the rather small space, a large machine and tanks will be in the way and there is some doubt as to the feasibility of a continuous supply of the gas tanks. It is estimated that with 3 operating teams, 20 major operations can be done in 24 hours in each trailer operating room. This trailer operating room will be accompanied by a sterilizer trailer, a kitchen trailer, and a power plant for electric current.

During use, the trailer operating room is backed up to an opening in a receiving ward tent. When all the casualties have been operated upon the trailers can move on to other fields, while doctors and nurses sent up

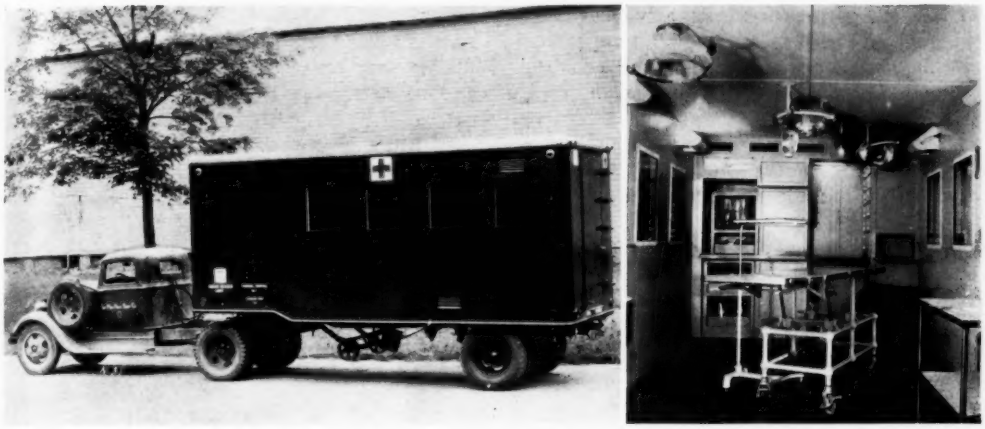

Fig. 1. Ambulance unit with interior view. (Reproduced through courtesy of Army Medical Museum.)

from the rear take over the now immobilized hospital, and the mobile units proceed to other localities.

At the Army Medical Center in Washington, D. C., we have a professional service school where all recently commissioned medical officers are sent for a 4 months' course of training in the principles of sanitation and preventative medicine, bacteriology and laboratory methods, and clinical instruction in orthopedic surgery. On completion of this course they are sent to the Medical Field Service School at Carlisle Barracks, Pennsylvania, where they receive 5 months' training in field work, practical sanitation, removal of wounded from the field, proper methods of preparation of patients for litter and ambulance transportation, and instruction in the handling of field hospitals and ambulance companies. On completion of this course they are ordered to various posts and general hospitals and have an opportunity to put to practical use the knowledge gained.

These young medical officers come from all parts of the United States, are graduates of reputable medical schools, and have interned in the best hospitals of the country; a fixed number each year apply for an interneship in some of our general and large station hospitals of the Army. Each man accepted is recommended by the dean of his college and reports to the specified hospital on June 30. The interneship, when completed, gives him the necessary credits for his graduation During their interneships these young doctors receive board, room, and 60 dollars a month. At the completion of their interneships and if recommended by the Medical Board, they are offered a commission as First Lieutenant in the Medical Corps of the Army. We secure many fine medical officers in this manner.

The Surgeon General, from time to time as vacancies occur or an increased quota of medical officers is authorized, announces dates for examination for commission in the Medical Corps. Examinations are held at various Army posts throughout the United States. Our physical examinations are very exacting as we hope each officer accepted will be physically qualified for at least 30 years' service.

During recent meetings in Washington, D. C., under the direction of the National Board of Research and the Surgeon Generals of the Army, Navy, and Public Health Service, well known physicians and surgeons called from all parts of the United States have started an intensive study of the better methods of treating battle casualties and handling respiratory and other infectious diseases. Dr. Evarts A. Graham is the chairman of the general committee and each member of the general committee is the chairman of a subcommittee for study of the

various types of regional surgery, anesthesia, chemiotherapy, etc. Each committee is getting together in manuals all data covering the best method of treating the region wounded, and in the event of war these manuals will be published in a concise form to outline the better procedures, so that a young surgeon may quickly review and follow them.

An example in the plastic maxillofacial manual would be: "*don't remove loosely attached bone fragments*. Support jaw with bandage and put an airway through the mouth. *Don't remove lacerated skin or muscles*. Save it for the plastic surgical team at the evacuation or fixed hospitals." Other manuals will give similar types of information. It is desirable that these manuals be of pocket size and on one page the *do's* and *don't's* summarized.

In conclusion, may I say that if any of my statements help the junior medical officer in finding his place in the Army, I shall feel well repaid.

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THE NATIONAL RESEARCH COUNCIL COMMITTEE ON SURGERY

A Brief Statement of Its Work

EVARTS A. GRAHAM, M.D., F.A.C.S., St. Louis, Missouri

ANYONE who recalls the confusion and the hysterical haste which were conspicuous features of the medical preparations of the last war will doubtless be relieved to learn that if war comes this time there will be a minimum of confusion. At the time of the last war practically no medical preparations were made until after we were actually engaged in the conflict. Now, however, active steps are being taken to prepare adequately the medical corps of the Army and Navy well beforehand.

To accomplish this preparation there has been a division of labor, and different tasks have been assigned to different organizations. I shall speak briefly of the National Research Council Committee on Surgery. First a few words about the National Research Council. In 1916, realizing that this country was likely to be drawn into the maelstrom of the European war, President Wilson organized the National Research Council to give to the Government such advice on scientific matters of various kinds as might be needed in a national emergency. Since the war the existence of the Council has been maintained. It consists of several divisions, of which one is that of the medical sciences; and it shares with the National Academy of Science the beautiful building at 21st Street and Constitution Avenue, Washington.

In May of this year, realizing that again the nation was confronted with the possible danger of war, the Surgeons General of the Army, the Navy, and the Public Health Service called upon the National Research Council for advice regarding the newer ideas on the prevention and treatment of shock and on the applicability of the newer chemotherapeutic drugs to war infections. The chairman of the Division of Medical Sciences, Dr. Lewis H. Weed, accordingly appointed some committees to investigate the particular problems. It was soon realized, however, that the advisory work should have a much wider scope than that upon which the original work was undertaken. At the present time, in addition to the two original committees on shock and on chemotherapy, respectively, there are three other major committees—one on surgery, one on medicine, and one on information. Of these major committees there are thirty subcommittees at work. The selection of the committees has been made after consultation with various civilian individuals and groups as well as with officials of the Army, Navy, and Public Health Service.

In order that there should be as little overlapping of function as possible the National Research Council's committees limit their activities to such fields as experimental research on problems that come up, matters of all kinds which concern the professional activities of the reserve medical officers personnel, advice on medical equipment and instruments, and in short anything with which the doctor as a medical officer is likely to be involved, aside from purely military or naval activities. As you know, the huge task of cataloging and classifying the medical profession of the country has been taken over by the American Medical Association. No other agency is so well equipped to carry out this function. We are fortunate that in this country at this time of peril to the nation there exists so efficient and powerful an organization able to perform this gigantic task of supplying to the armed forces of our country a list of experts available for every conceivable kind of medical work. The National Research Council Committee on Surgery is cooperating with the American Medical Association Committee to facilitate this work as much as possible. As a result of the careful evaluation and appraisal of each doctor's abilities, it is expected that there will be far fewer round pegs in square holes than in the last war. There will be no opportunity for any doctor, merely on the basis of wishful thinking, to be recognized by the army as a specialist. The committees which will scrutinize his record and assign him accordingly to his proper place will be guided only by his training and performance. Recently another much needed committee has been organized of which our own Dr. Abell is chairman. It has been recognized for several months that a committee to deal with all

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those affairs which will concern the health and medical activities of the civilian population in case of war should be organized as a part of the Council of National Defense, and recently President Roosevelt has appointed such a committee. Dr. Abell himself will tell you more of this committee. I may say, however, in order to emphasize the harmony and co-operation with which the various medical preparedness committees are working, that Dr. Abell besides being chairman of this last mentioned committee is also chairman of the American Medical Association committee and a member of the National Research Council Committee on Surgery.

As examples of the sort of work that is being done by the National Research Council Committee on Surgery, besides what has already been mentioned, it may be said that an extensive program of research on surgical infections is about to begin. Various pocket manuals of instruction of how to deal with different kinds of wounds are being prepared. Consideration is being given to the use of more protective armor than the steel helmet. The most suitable methods of anesthesia for different kinds of operations and for use in different kinds of hospitals, together with the various types of anesthesia apparatus, are being discussed. Similar considerations are being given to the use of the x-ray under the varying conditions of warfare. Many research projects are being given consideration, some of which will probably be set in motion soon. These are only some of the activities of that committee. We are not concerned with the granting of commissions in the reserve corps to any individuals except through our co-operation with the American Medical Association in the evaluation of the qualifications of individual specialists. We have, however, expressed the hope that the course of training of the young surgeons will not be seriously interrupted and that the work of the civilian hospitals will not be crippled by a wholesale removal of the house-staffs for military purposes. There is good reason to think that this hope which is shared by all who have an intelligent appreciation of the needs of the hospitals will be realized.

TWENTY-THIRD ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

MALCOLM T. MacEACHERN, M.D., Chicago, Illinois

HOSPITAL Standardization is an exceedingly involved activity which nevertheless it is possible to crystallize in a single expression of its progress every year—the "Approved List." The announcement of the list of 2,806 approved hospitals at the twenty-third annual Hospital Standardization Conference, held in Chicago in October, 1940, and its publication in the approval number of the College *Bulletin*, may seem to the uninformed observer to have been routine procedures, which have lost their stimulating effect because of the many regular repetitions. Instead, issuance of the list seems to acquire added significance each year, to judge by the repercussions that follow from the borderline hospitals which expected to be included but were not, and by the inquiries about how to meet the requirements some of which come from hospitals which were scarcely considered even as aspiring to approval.

Some things there are upon which steady hammering away with expression of ideals and the citing of examples creates an interest more substantial than that which is won by novelty. Hospital Standardization has earned a place in this category. Its influence has been cumulative. While it is true that a great many hospitals occupy an assured position on the approved list, that a doubt never arises about finding their names on it year after year, nevertheless even upon them the activity has a constantly stimulating effect because the fact of reconsideration for approval each year makes it necessary for them consciously to keep abreast of improvements in all phases of hospital work. Every year it becomes an unpleasant necessity to omit from the list some hospital from which protest is made on the sole ground that it has been approved for 10 or 15 years, and its facilities and methods are as good as they were when approval was granted. The answer to that protest is that the interpretation of the Minimum Standard is progressive from year to year, and that in the march of progress the hospital that is static falls farther and farther to the rear until finally it is behind the vanguard of approved hospitals and deserves no place in their ranks. Though a hospital has been twenty times approved, it has no assurance that it will be approved the twenty-first year unless it is positive that in every respect it is up-to-date as of the current period in the advance of hospitals.

Of course, a great satisfaction in hospital standardization work is the handful of hospitals that are each year converted from the borderline condition to full acceptance of the standard. The satisfaction does not lie in being able to show an increase in the number of approved hospitals, but in making available to more patients the benefits of hospital service that is properly organized, controlled, and directed. Whenever a hospital is added to the approved list, the correct way to evaluate the gain is by the additional number of patients who are as a consequence receiving better care. Patients in the smaller hospitals and in hospitals in areas distant from the medical centers are especially in need of the assurance that they are receiving a high quality of care, and this assurance the approved hospital is entitled to give.

So far as the smaller town is concerned, Hospital Standardization has been a timely activity, coincident with a rapid general trend toward better distribution of the comforts, conveniences, safeguards, and luxuries of life. In a recent article in *Harper's Magazine* by Bernard De Voto on "Main Street Twenty Years After," an excellent description is given of the way in which standardization has transformed the average town. Retail stores, schools, transportation and communication systems, power and light facilities, and sanitary precautions, have been immeasurably improved through standardization even in small villages. Hospital service should have kept pace with this advance, and it is the aim of Hospital Standardization that at least the same favorable comparison with facilities in the large cities be attained by the hospitals as by other public services in the smaller communities. Not all of the unapproved hospitals are by any means in the less populous areas, it is true, but so large a proportion of them are that the need there should be emphasized. De Voto says that standardization, "which so enraged the intellectuals of the 1920's, has in reality annihilated much that was deadening and disruptive in rural existence." To which should be added that it has also annihilated

much that was distressing and dangerous, when sickness or accident struck, by making it possible for a hospital to give good service even when its capacity is as few as 25 beds.

Hospital Standardization is not only always reaching out to influence for good the below grade hospital, but it is also working for better service to the individual patient in the approved hospitals. A hospital that readily meets the general standards for approval, may yet be ministering poorly to the needs of certain types of patients. These needs are discovered in the surveys and through contacts with hospital personnel who are aware of them, and are brought up for discussion at the Hospital Standardization Conferences in connection with the Clinical Congress and sectional meetings of the College. An example was the conference on convalescent care at the Clinical Congress in October in which the needs of a number of different types of convalescent patients were discussed by specialists in each field. The keynote was set by the title of the address of the presiding officer, Dr. Harry E. Mock, of Chicago, "Convalescent Care—the Missing Link in the Cure of Many Patients." The special needs of the surgical, the medical, the cancer, the fracture, the orthopedic, and the pediatric patient were presented, respectively, by Dr. Donald B. Wells, of Hartford; Dr. Newell C. Gilbert, of Chicago; Dr. Frank E. Adair, of New York; Dr. Robert H. Kennedy, of New York; Dr. Frederick C. Kidner, of Detroit; and Dr. Louis A. Schwartz, of Detroit. Dr. Gilbert made a particularly salient point when he departed from the idea of "convalescence" toward that of using the convalescent home partly as a "preventorium," urging that hospitalization could frequently be avoided, with great economic saving, by preventive care in this type of institution. Dr. William H Walsh, of Chicago, in describing the essentials in planning of institutions for convalescent care, said that surveys have shown that an average of 12 per cent of patients occupying beds for acute illness in hospitals are suitable cases for convalescent care, and remarked that "if and when adequate convalescent facilities are made available, there will be a considerable reduction in the number of chronic cases to be provided for." Elizabeth G. Gardiner, of New York, in a talk on "Socio-Economic Aspects of Convalescent Care," urged the increased consideration of proper convalescent care as a means of more speedily returning the patient to his or her usual function as worker or housewife. E. H. L. Corwin, Ph.D., of New York, in discussing "Minimum Standards for Convalescent Hospitals," suggested that "with the oncoming national emergency it may be of great moment to be able to transfer to convalescent homes, hospital patients who have passed the acute stage of their illness or disability," and he therefore urged that the American College of Surgeons "duplicate the splendid work it has done in the hospital field by developing minimum standards for convalescent hospitals and supervising their adoption," saying that, after all, "the medical and surgical job is not completed upon the patient's discharge from the hospital."

It may well be that the needs of the national defense program as it concerns hospitals will indicate the desirability of more attention to the needs of the convalescent patient, and will act as a spur to greater development of facilities to serve him. The Minimum Standard for Hospitals is sufficiently elastic to provide a gauge of approval for the convalescent institution, and if after further study and investigation it seems desirable to formulate as a guide a special auxiliary minimum standard, this can readily be done as it was in the case of cancer clinics and of plans for graduate training in surgery in hospitals.

The Hospital Standardization conferences are valuable in bringing new needs to the surface and in enabling exchange of views with hospital personnel on current problems. They, together with the personal surveys on which the approved list is based, keep Hospital Standardization close to the ground, broadening its scope to embrace developing needs, and making approval a practical, attainable goal for any hospital and a direct influence for better service to every patient.

THE 1940 CLINICAL CONGRESS

JOHN A. WOLFER, M.D., F.A.C.S., Chicago, Illinois

SOME dominant note in response to a scientific development or a social need seems to ring through each Clinical Congress, and, as might have been expected, the 1940 Congress was tuned to the current interest in national defense. Though in only one session were the discussions predominantly centered upon the physician's rôle in military preparedness, nevertheless the additional incentive for research and experimentation, which preparedness gives, kept rising to the surface in the talks and comments at many of the meetings. A report on the work and plans of the committee on surgery of the National Research Council was presented by its chairman, Dr. Evarts A. Graham, the new president of the American College of Surgeons, and the aims of the health and medical committee of the Council of National Defense to co-ordinate the efforts of all agencies working for medical preparedness were described by its chairman, Dr. Irvin Abell, chairman of the Board of Regents, at the Wednesday evening session. Representing the medical corps of the United States Army, Brigadier General Raymond F. Metcalfe told of the correct attitude of medical officers toward draftees, and described some of the applications in military service of new developments in medicine.

The Surgeon General of the United States Navy, Rear Admiral Ross T. McIntire, brought to the attention of the public the plans for "Medical Preparedness for National Defense" in an address sponsored by the College over the National Broadcasting Company network on Sunday evening preceding the opening of the Clinical Congress. Introduced by Dr. Abell, Admiral McIntire said in part:

"It is extremely gratifying to find the splendid co-operation that is being given to the Army and the Navy by such organizations as the American College of Surgeons. The work of the College in the industrial field of medicine is playing a most important part in plans for expansion in that field. . . . The Army and the Navy will demand a great deal from the medical profession, the nurses, the hospitals, and all other allied organizations that have to do with health. We in the military services are being exceedingly careful not to rob our industrial centers, our small towns, and rural communities of proper medical and hospital care.

"This is being done by the preparation of a broad and comprehensive plan by which proper selection of personnel will be made in a rational manner."

Chairman of the Committee on Arrangements.

Brigadier General Metcalfe gave a talk over the Columbia Broadcasting System network on Thursday evening of the Congress in which, following an introduction by Dr. Graham, he told of a preparedness program, "not for war, but to prevent war," and assured the mothers of America that their sons, if called to military service, will receive "good food, warm clothing, healthful training, instruction in a particular branch of service, instruction in personal hygiene, and the best of medical care if sick or injured."

Particular mention is made of these broadcasts because of the omission from the 1940 Clinical Congress program of the heretofore customary community health meeting, and because the chairman of the arrangements committee is also chairman of the Committee on Public Relations and hence is immediately concerned with those aspects of the Congress which are of interest to the public as well as those that appeal to the profession. Through the co-operation of the public service divisions of the large broadcasting systems it was possible to convey to the public the timely messages of the Surgeon General of the Navy and the assistant to the Surgeon General of the Army.

The 1940 Presidential Meeting or Convocation was lacking, of necessity, in one feature to which we have become accustomed, the introduction of foreign guests, but in other respects was characterized by the usual impressiveness. The class of initiates received into fellowship was exceptionally large—there was a total of 611 new members—which brings the enrollment of the Fellows to well over 13,000.

The clinics in some forty of the approved hospitals in the Chicago area were exceptionally well attended, and again it was demonstrated how helpful it is to the individual surgeon to have the program so arranged that one who is interested in a specialty can if he wishes give almost undivided time to its study in the clinics and in the scientific sessions, panel discussions, and group clinical conferences. The clinical conferences were a new feature in 1940, and a popular one, with overflow attendance registered in many instances. The ophthalmologists and otorhinolaryngologists, in particular, expressed great satisfaction with the six conferences arranged for them on three successive mornings.

The symposium on cancer attracted the usual wide interest, and considered in conjunction with the announcement of the list of 345 approved cancer clinics in hospitals in the United States and Canada, and of additions to the archives of 5-year cancer cures which bring the total to 36,078, constituted one of the most important events of the Congress, indicating the concentrated effort that is being directed toward gaining better control of this disease.

Another outstanding session was the symposium on fractures and other traumas. This session, also, should be evaluated against its background of intensive activity by the College, especially in connection with the treatment of fractures which has been improved largely through the efforts of the Committee on Fractures and the Regional Fracture Committees which, the chairman of this meeting announced, now number 85 and have a total membership of 1,400.

The reports of the Committee on Cancer and of the Committee on Fractures and Other Traumas were presented in detail at the annual meeting of the Fellows on Thursday afternoon, together with reports of the Library and Department of Literary Research, the Department of Hospital Standardization, the Department of Clinical Research, and others, giving an impressive picture to the Fellows of the great amount of activity bearing directly upon improvement of medical and hospital service in which the College is engaged.

As to new developments reported at the Congress, that in which there is probably the widest interest was the increasing use of the sulfonamides; one speaker told of the use of these compounds as aids to surgery, and another described the rapid healing of wounds received in war or accidents when sulfanilamide was applied. Another interesting report was that the acute symptoms of Ménière's disease may be relieved by injections of histamine. The permanent cure of Ménière's disease by dividing the auditory nerve was reported in 401 operations, with only 1 death which was due to meningitis. The use of the anti-blood-clotting substance, heparin, in the successful grafting of pieces of veins to bridge gaps in wound-torn arteries was announced. The results of high voltage radiation therapy in gynecological cancer were reported.

The 1940 Congress brought forth many new ideas in applying the scientific developments in practice in hospitals. The concurrent holding of hospital conferences serves to emphasize the important place of surgery in the hospital and the desirability of its strict control. It serves also to keep before the surgeon's mind the many services in the hospital, proper performance of which contributes to more successful surgery.

The surgeons of Chicago are proud to have been hosts to the thirtieth Clinical Congress, as they were to the first, held in 1910. Eight times our city has been the setting for this illustrious gathering. The medical schools and hospitals of Chicago co-operated generously in arrangements for the 1940 meeting, and the committee gratefully acknowledges their support and that of the individual speakers, leaders of discussion and collaborators, exhibitors, and all who in any way helped toward the success of the Congress.

FUTURE NEEDS FOR GRADUATE TRAINING IN GENERAL SURGERY AND THE SURGICAL SPECIALTIES

DALLAS B. PHEMISTER, M.D., F.A.C.S., Chicago, Illinois

IN its program of graduate training in surgery the American College of Surgeons has proceeded on the theory that all hospitals, be they large or small, situated in metropolitan centers or in the smaller towns, are educational institutions in the truest sense when they follow the principles of hospital standardization. The medical school lays the foundation for the education of the physician, but the hospital erects upon that foundation the framework of practical training. In proportion as the educational rôle of the hospital is conscientiously planned and played, the physicians and surgeons who enter practice will be competent and trustworthy.

The medical schools alone, important and fundamental as their place is, can never produce surgeons sufficiently qualified to be entrusted with people's lives. Apprenticeship to an older practitioner is now less and less frequently employed as a method of training. Hence in our day the hospital, every hospital, must definitely assume its due share of teaching responsibility if the public are to be given the full advantages of progress in medical science. This is a never ending responsibility, not only in respect to the year by year entrance and outgoing of internes and residents, but in its application to the progressive education of every member of the staff. Even the hospital that has no internes or residents may so organize its staff that there is effective control by the more experienced members over those not so well qualified, and this is an educational function.

What the College hopes to do, and what it has already in some degree accomplished, is to heighten the consciousness of hospitals to their educational obligations and opportunities. The graduate training program is simply hospital standardization carried forward in one of its educational phases. Rather conspicuous proof of success in arousing a consciousness of educational responsibility was furnished by the publication in the October, 1940, *Bulletin*, of detailed descriptions of the plans for graduate training in general surgery and the surgical specialties of two hundred hospitals in the United States and Canada which have been approved for this purpose. Many hospitals have initiated graduate training programs, and others have amplified and revised theirs, as a result of encouragement by the College, and guidance which in the past year has taken tangible form in a published *Manual*, available now in reprint form under the same cover with the descriptions of the approved plans.

Chairman of the Committee on Graduate Training for Surgery.

The growth in the number of hospitals participating in approved plans from 179 on October 1, 1939, to 200 on October 1, 1940, together with the increase in the number of men in training in general surgery and the surgical specialties from 1,606 in 1939 to 1,745 in 1940, shows the widening interest. There is also indicated a definite trend toward development of plans of graduate training of three or more years' duration in general surgery, as well as in many of the surgical specialties, that is significant. Of those completing work in general surgery in 1940, 73 per cent received three or more years' training.

A number of the hospitals whose plans for graduate training in surgery have been approved are a part of universities and medical schools. Valuable as such direct connections are in facilitating study of the basic sciences, a lack of them and also of sufficient and varied clinical material can be surmounted by affiliation with some medical school and by co-operation with other hospitals. So thoroughly convinced is the College by its experience with this program that the standards of surgical performance in a hospital are almost automatically raised when it undertakes to provide graduate training in surgery, that the theory upon which future work will be based is that reasonably wide participation is eminently desirable, and encouragement and help will continue to be given the hospital which establishes affiliations in order to furnish a well rounded program.

Better distribution of thoroughly qualified surgeons is the great need, and an obvious way of helping to effect this is to have surgical training centers more widely distributed. Some of those who complete their training in districts away from the leading medical centers will remain there to practice, and not only the institutions definitely organized for teaching, but others in the vicinity as well, will benefit ultimately by having better surgeons on their staffs. The cycle of benefits will

be advanced by the attraction of surgeons trained in the medical centers, to the improved hospitals in the less populous areas.

It is a long view that the College is taking in the graduate training program—a view that yields no prospect of a goal possible of complete attainment. To the argument that enough surgeons are being trained now to fill the need in numerical terms, the conclusive answer is that not all of these surgeons are being trained well enough, nor are there likely to be too many well trained surgeons, at least in the generations immediately ahead of us. For medical schools a curriculum can be established, adherence to which forms the basis of approval; for hospitals so many intangible factors are involved in addition to provisions for basic science study and supervision, that constant and continuous work with them is essential to progress. This is especially true in view of the fact that, after all, the teaching function is subordinate to the chief purpose of serving the patient and is worthy of promotion only because, when properly carried out, it contributes to improvement in that primary aim.

The program is an integral part of the purpose of the College to elevate the standards of surgery. It is notable for interpreting that purpose to mean that the standards should be elevated everywhere. Because the need for better surgery is greatest in that type of institution, the keenest satisfaction is felt when the heretofore "non-teaching" hospital assumes teaching and training responsibilities and meets the requirements for approval. The College has closely at heart the welfare of patients in all types and sizes of hospitals and is constantly striving for higher standards of training for surgeons and better control of surgery.

Hospital standardization and graduate training for surgery, as well as for all other branches of medicine, should progress hand in hand. No hospital of the requisite bed capacity should be recognized as possessing adequate standards which does not also conduct a program for adequate training for surgery.

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The Thirty-first Annual Clinical Congress of the American College of Surgeons will be held in Boston November 3–7, 1941.

CLINICAL CONGRESS TECHNICAL EXHIBITION

LEADING manufacturers of and dealers in surgical instruments, hospital apparatus and supplies, diagnostic and therapeutic apparatus, pharmaceuticals, and publishers of medical and surgical books were represented in the Technical Exhibition at the Stevens Hotel in Chicago, October 21–25, 1940.

W. D. Allison Co., Indianapolis
A. S. Aloe Co., St. Louis
American Cystoscope Makers, Inc., New York
American Hospital Supply Corp., Chicago
American Journal of Surgery, New York
American Safety Razor Corp., Brooklyn
American Sterilizer Co., Erie, Pa.
D. Appleton-Century Co., New York
Armour & Co., Chicago
Austenal Laboratories, New York
Aznoe's National Physicians' Exchange, Chicago
C. R. Bard, Inc., New York
Bard-Parker Co., Danbury, Conn.
W. A. Baum Co., Inc., New York
Baxter Laboratories, Glenview, Ill.
Becton, Dickinson & Co., Rutherford, N. J.
Bell & Howell, Chicago
Julius Berbecker & Sons, New York
Birtcher Corp., Los Angeles
Blakiston Co., Philadelphia
Burdick Corp., Milton, Wis.
Burrows Co., Chicago
S. H. Camp & Co., Jackson, Mich.
Wilmot Castle Co., Rochester, N. Y.
Gilbert Hyde Chick Co., Berkeley, Calif.
Cilkloid Co., Marshalltown, Iowa
Clay-Adams Co., New York
Warren E. Collins, Inc., Boston
Comper Manufacturing Co., Pittsfield, Mass.
Conformal Footwear Co., St. Louis
Crane Co., Chicago
Crescent Surgical Sales Co., New York
Cutter Laboratories, Berkeley, Calif.
R. B. Davis Sales Co., Hoboken, N. J.
Davis & Geck, Brooklyn
J. A. Deknatel & Son, Queens Village, N. Y.
DePuy Manufacturing Co., Warsaw, Ind.
A. W. Diack, Detroit
Duke Laboratories, Stamford, Conn.
Eastman Kodak Co., Rochester, N. Y.
E & J Co. of Pennsylvania, Philadelphia
J. H. Emerson Co., Cambridge, Mass.
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General Electric X-Ray Corp., Chicago
Gudebrod Bros. Silk Co., Philadelphia
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Hospital Liquids, Inc., New York
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Lea & Febiger, Philadelphia
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Liebel-Flarsheim Co., Cincinnati
Eli Lilly & Co., Indianapolis
J. B. Lippincott Co., Philadelphia
MacGregor Instrument Co., Boston
Majestic Surgical Instrument Co., Chicago
Massillon Rubber Co., Massillon, Ohio
McKesson Appliance Co., Toledo
Medical Bureau, Chicago
Merck & Co., Rahway, N. J.
C. V. Mosby Co., St. Louis
V. Mueller & Co., Chicago
New York Medical Exchange, New York
Ohio Chemical & Manufacturing Co., Cleveland
Oxford University Press, New York
Oxygen Equipment & Service Co., Chicago
Petrolagar Laboratories, Chicago
Physicians' Record Co., Chicago
Picker X-Ray Corp., New York
W. F. Prior Co., Hagerstown, Md.
Prometheus Electric Corp., New York
Puritan Compressed Gas Co., Kansas City, Mo.
Radium Chemical Co., Inc., New York
Radium Emanation Corp., New York
Richards Manufacturing Co., Memphis, Tenn.
Ritter Equipment Co., Rochester, N. Y.
Safety Gas Machine Co., Chicago
Sanborn Co., Cambridge, Mass.
W. B. Saunders Co., Philadelphia
Scanlan-Morris Co., Madison, Wis.
Schering Corp., Bloomfield, N. J.
Schering & Glatz, New York
J. R. Siebrandt Manufacturing Co., Kansas City, Mo.
J. Sklar Manufacturing Co., Long Island City, N. Y.
Smith, Kline & French Laboratories, Philadelphia
Smith & Nephew, New York
C. M. Sorenson Co., Long Island City, N. Y.
E. R. Squibb & Sons, New York
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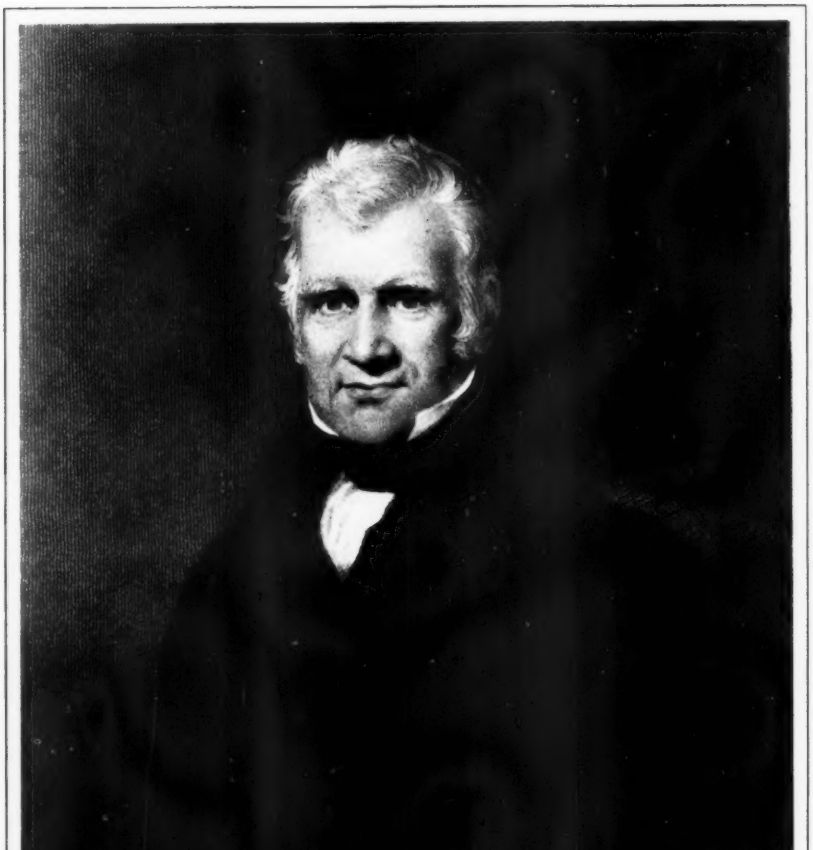
HENRY CLUTTERBUCK (1767–1856). Surgeon and physician; courageous defender of medical ethics; the most effective lecturer on materia medica and the practice of physic in London; author of "Inquiry into the Seat and Nature of Fever," 1809.



Henry Clutterbuck

1767-1856